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# THE HARRIET LANE HANDBOOK

TWENTIETH EDITION

BRANDEN ENGORN

JAMIE FLERLAGE

ELSEVIER  
S.A.U.



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PEDIATRIC PARAMETERS AND EQUIPMENT									
	premie	new born	6 MO	1 YR	2-3 YR	4-6 YR	7-10 YR	11-15 YR	>16 YR
WT (KG)	2.5-3.5 kg	3.5-4 kg	6-8 kg	10 kg	13-16 kg	20-25 kg	25-35 kg	40-50 kg	>50 kg
BAG/VALVE MASK	Infant	Infant	Small Child	Small Child	Child	Child	Child/S. Adult	Adult	Adult
NASAL AIRWAY	12 Fr	12 Fr	14-16 Fr	14-16 Fr	14-18 Fr	14-18 Fr	16-20 Fr	18-22 Fr	22-36 Fr
ORAL AIRWAY	Infant 50 mm	Small 60 mm	Small 60 mm	Small 60 mm	Small 70 mm	Small 70-80 mm	Med 80-90 mm	Med 90 mm	Med 90 mm
BLADE	MIL 0	MIL 0	MIL 1	MIL 1, MAC 2	MIL 1, MAC 2	MIL 2, MAC 3	MIL 2, MAC 3	MIL 2, MAC 3	MIL 2, MAC 3
ETT	2.5-3.0	3.0-3.5	3.5-4.0	4.0-4.5	4.5-5.0	5.0-5.5	5.5-6.0	6.0-6.5	7.0-8.0
LMA	1	1	1.5	2	2	2.5	2.5-3	3	4
GLIDESCOPE	1	1 or 2	2	2	3	3	3	3 or 4	3 or 4
IV CATH	22-24 ga	22-24 ga	20-24 ga	20-24 ga	18-22 ga	18-22 ga	18-22 ga	18-20 ga	16-20 ga
CVL	3 Fr	3-4 Fr	4 Fr	4-5 Fr	4-5 Fr	5 Fr	5 Fr	7 Fr	7 Fr
NGT/OGT	5 Fr	5-8 Fr	8 Fr	10 Fr	10-12 Fr	12-14 Fr	12-14 Fr	14-18 Fr	14-18 Fr
CHEST TUBE	10-12 F	10-12 Fr	12-18 Fr	16-20 Fr	16-24 Fr	20-28 Fr	20-32 Fr	28-38 Fr	28-42 Fr
FOLEY	6 Fr	8 Fr	8 Fr	8 Fr	8 Fr	8 Fr	8 Fr	10 Fr	12 Fr
ESTIMATED BLOOD PRESSURE BY AGE									
MEASUREMENT	50th %				5th %				
Systolic BP	90 + (age x 2)				60 (neonate); 70 (1mo-1 yr) 70 + (age x 2) (for 2-10 yrs) <90 (>10 yrs)				
MAP	55 + (age x 1.5)				40 + (age x 1.5)				
NORMAL VITAL SIGNS BY AGE									
Age	HR (beats/min)		BP (mm Hg)				RR (breaths/min)		
Premie	120-170		55-75/35-45 (gestational age approximates nml MAP)				40-70		
0-3 mo	110-160		65-85/45-55				30-60		
3-6 mo	100-150		70-90/50-65				30-45		
6-12 mo	90-130		80-100/55-65				25-40		
1-3 yrs	80-125		90-105/55-70				20-30		
3-6 yrs	70-115		95-110/60-75				20-25		
6-12 yrs	60-100		100-120/60-75				14-22		
>12 yrs	60-100		100-120/70-80				12-18		
ENDOTRACHEAL TUBE FORMULAS									
Uncuffed ETT size: age (years)/4 +4; Cuffed ETT size: age (years)/4 +3 ETT depth (from lip to mid-trachea): ETT internal diameter (size) x 3									

## GLASGOW COMA SCALE

Activity	Score	Child/Adult	Score	Infant
Eye opening	4	Spontaneous	4	Spontaneous
	3	To speech	3	To speech/sound
	2	To pain	2	To pain
	1	None	1	None
Verbal	5	Oriented	5	Coos/babbles
	4	Confused	4	Irritable cry
	3	Inappropriate	3	Cries to pain
	2	Incomprehensible	2	Moans to pain
	1	None	1	None
Motor	6	Obeys commands	6	Normal spontaneous
	5	Localizes to pain	5	Withdraws to touch
	4	Withdraws to pain	4	Withdraws to pain
	3	Abnormal flexion	3	Abnormal flexion (decorticate)
	2	Abnormal extension	2	Abnormal extension (decerebrate)
	1	None	1	None

Adapted from Hunt B, Nelson K. The Johns Hopkins Children's Center Kids Kard, 2014.

$$\text{IV INFUSIONS}^* \quad 6 \times \frac{\text{Desired dose (mcg/kg/min)}}{\text{Desired rate (mL/hr)}} \times \text{Wt (kg)} = \frac{\text{mg drug}}{100 \text{ mL fluid}}$$

Medication	Dose (mcg/kg/min)	Dilution in 100 mL D <sub>5</sub> W	IV Infusion Rate
Alprostadil (prostaglandin E <sub>1</sub> )	0.05–0.1	0.3 mg/kg	1 mL/hr = 0.05 mcg/kg/min
Amiodarone	5–15	6 mg/kg	1 mL/hr = 1 mcg/kg/min
DOPamine	2–20	6 mg/kg	1 mL/hr = 1 mcg/kg/min
DOBUTamine	2–20	6 mg/kg	1 mL/hr = 1 mcg/kg/min
EPINEPHrine	0.1–1	0.6 mg/kg	1 mL/hr = 0.1 mcg/kg/min
Lidocaine	20–50	6 mg/kg	1 mL/hr = 1 mcg/kg/min
Phenylephrine	0.05–2	0.3 mg/kg	1 mL/hr = 0.05 mcg/kg/min
Terbutaline	0.1–10	0.6 mg/kg	1 mL/hr = 0.1 mcg/kg/min
Vasopressin (pressor)	0.5–2 milliunits/kg/min	6 milliunits/kg	1 mL/hr = 1 milliunit/kg/min

\* Standardized concentrations are recommended when available.

## RESUSCITATION MEDICATIONS

<b>Adenosine</b> Supraventricular tachycardia	<b>0.1 mg/kg IV/IO RAPID BOLUS (over 1-2 sec), Flush with 10 mL normal saline</b> May repeat at 0.2 mg/kg IV/IO after 2 min Max first dose 6 mg, max subsequent dose 12 mg
<b>Amiodarone</b> Ventricular tachycardia Ventricular fibrillation	<b>5 mg/kg IV/IO</b> No Pulse: Push Undiluted Pulse: Dilute and give over 30 minutes Max first dose 300 mg, max subsequent dose 150 mg Monitor for hypotension
<b>Atropine</b> Bradycardia (increased vagal tone) Primary AV block	<b>0.02 mg/kg IV/IO, 0.04–0.06 mg/kg ETT</b> Max single dose 0.5 mg Repeat once if needed
<b>Calcium chloride (10%)</b> Hypocalcemia	<b>20 mg/kg IV/IO</b> Max dose 1 g
<b>Dextrose</b>	<b>&lt;5 kg: 10% dextrose 10 mL/kg</b> <b>5–44 kg: 25% dextrose 4 mL/kg</b> <b>≥45 kg: 50% dextrose 2 mL/kg, max single dose 50 g = 100 mL</b>
<b>Epinephrine</b> Pulseless arrest Bradycardia (symptomatic) Anaphylaxis	<b>0.01 mg/kg (0.1 mL/kg) 1:10,000 IV/IO every 3–5 min (max single dose 1 mg)</b> <b>0.1 mg/kg (0.1 mL/kg) 1:1000 ETT every 3–5 min (max single dose 2.5 mg)</b> <b>Anaphylaxis: 0.01 mg/kg (0.01 mL/kg) of 1:1000 IM (max 0.5 mg) in thigh every 15 min PRN</b> <b>Standardized/Autoinjector:</b> <b>&lt;10 kg: 0.01 mg/kg (0.01 mL/kg) of 1:1000 IM</b> <b>10–30 kg: 0.15 mg IM</b> <b>&gt;30 kg: 0.3 mg IM</b>
<b>Insulin (Regular or Aspart)</b> Hyperkalemia	<b>0.1 units/kg IV/IO with 1 g/kg of dextrose</b> Max single dose 10 units
<b>Magnesium sulfate</b> Torsades de pointes Hypomagnesemia	<b>50 mg/kg IV/IO</b> No Pulse: Push Pulse: Give over 15–20 minutes Max single dose 2 g Monitor for hypotension/bradycardia
<b>Naloxone</b> Opioid overdose Coma	<b>Respiratory Depression: 0.001–0.005 mg/kg/dose IV/IO/IM/SubQ (max 0.08 mg first dose, may titrate to effect)</b> <b>Full Reversal/Arrest Dose: 0.1 mg/kg IV/IO/IM/SubQ (max dose 2 mg)</b> ETT dose 2–3 times IV dose. May give every 2 min PRN
<b>Sodium Bicarbonate (8.4%)</b> Metabolic acidosis Hyperkalemia Tricyclic antidepressant overdose	<b>1 mEq/kg IV/IO</b> Dilute 1:1 with sterile water for <10 kg Hyperkalemia: Max single dose 50 mEq
<b>Vasopressin</b>	<b>0.5 units/kg/dose IV/IO</b> Max single dose 40 units

ETT Meds (NAVEL: naloxone, atropine, vasopressin, epinephrine, lidocaine)—dilute meds to 5 mL with NS, follow with positive-pressure ventilation. Special thanks to LeAnn McNamara and Angela Helder, Clinical Pharmacy Specialists, for their expert guidance with IV infusion and resuscitation medications guidelines.

Adapted from Hunt B, Nelson K. The Johns Hopkins Children's Center Kids Kard, 2014, and the American Heart Association, PALS Pocket Card, 2010.

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EDITION

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# THE HARRIET LANE HANDBOOK

*A Manual for Pediatric House Officers*



JOHNS HOPKINS  
CHILDREN'S CENTER

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TWENTIETH  
EDITION

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# THE HARRIET LANE HANDBOOK

*A Manual for Pediatric House Officers*

The Harriet Lane Service at  
The Charlotte R. Bloomberg Children's Center of  
The Johns Hopkins Hospital

## **EDITORS**

**Branden Engorn, MD**  
**Jamie Flerlage, MD**

**ELSEVIER**  
SAUNDERS



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**To all who use this book**

May the work you do better the lives  
of children everywhere.

**To our patients**

May we serve you well and learn  
from you each day.

**To our families**

To Anne and Bob Laubisch and my  
entire family, thank you for your endless  
encouragement in my life that has allowed  
me to follow my dreams.

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to work hard and never give up, and that  
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and the bad times.

**To our spouses**

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and for that I am forever grateful.

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wonderful wife and best friend,  
coming home to you is the perfect  
ending to every day.

**To our mentors**

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your mentorship has shaped our lives  
and that you are the physician  
we will always strive to be.

To George Dover, The Johns Hopkins  
Children's Center will forever be indebted  
to you for all the love, compassion,  
dedication, and time that you have given  
to enhance the lives of countless children  
and families.

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# Preface

*"Why this child? Why this disease? Why now?"*

—Barton Childs, MD

*The Harriet Lane Handbook* was first developed in 1953 after Harrison Spencer (chief resident in 1950–1951) suggested that residents should write a pocket-sized “pearl book.” As recounted by Henry Seidel, the first editor of *The Harriet Lane Handbook*, “Six of us began without funds and without [the] supervision of our elders, meeting sporadically around a table in the library of the Harriet Lane Home.” The product of their efforts was a concise yet comprehensive handbook that became an indispensable tool for the residents of the Harriet Lane Home. Ultimately, Robert Cooke (department chief, 1956–1974) realized the potential of the handbook, and, with his backing, the fifth edition was published for widespread distribution by Year Book. Since that time, the handbook has been regularly updated and rigorously revised to reflect the most up-to-date information and clinical guidelines available. It has grown from a humble Hopkins resident “pearl book” to become a nationally and internationally respected clinical resource. Now translated into many languages, the handbook is still intended as an easy-to-use manual to help pediatricians provide current and comprehensive pediatric care.

Today, *The Harriet Lane Handbook* continues to be updated and revised by house officers for house officers. Recognizing the limit to what can be included in a pocket guide, additional information has been placed online and for use via mobile applications.

This symbol  throughout the chapters denotes online content in Expert Consult. The online-only content includes expanded text, tables, additional images, and other references.

In this edition, the following are just a few examples of the changes made to enhance the usefulness of the book, decrease the weight of white coat pockets everywhere, and reflect changes made in guidelines and management since the nineteenth edition of the *The Harriet Lane Handbook*:

- Most notable, the **cover** has been changed from its traditional picture of the Johns Hopkins Dome to a photo of our new home, The Charlotte R. Bloomberg Children’s Center. The change for this edition commemorates 100 years since the opening of the Harriet Lane Home, 20 editions of *The Harriet Lane Handbook*, and the beginning of the next century of pediatric care at Johns Hopkins Hospital.
- In the **Development, Behavior, and Mental Health** chapter, the content has been updated to reflect the changes in the new *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition, most notably the diagnostic criteria for intellectual disability.
- In the **Procedures** chapter, links to the *New England Journal of Medicine* “Videos in Clinical Medicine” were added to the online content. Images for various procedures were updated.

- In the **Trauma, Burns, and Common Critical Care Emergencies** chapter, new additions include practice parameters for pediatric and neonatal septic shock as well as guidelines for the acute management of severe traumatic brain injury.
- The **Genetics** chapter has been divided for usability into two sections, metabolism and dysmorphology, and a table of collection information for common genetic tests was added.
- The photo atlas in the **Radiology** chapter has been expanded and improved.
- The majority of the **Formulary Adjunct** chapter content was moved to the relevant chapters.

*The Harriet Lane Handbook*, designed for pediatric house staff, was made possible by the extraordinary efforts of this year's senior resident class, the members of which balanced their busy schedules with authoring the chapters that follow. We are grateful to each of these residents along with their faculty advisors, who selflessly dedicated their time to improve the quality and content of this publication. The spirit of this handbook is our residents, who are the heart and soul of our department.

Chapter Title	Resident	Faculty Advisor
1. Emergency Management	Stephanie Chin-Sang, MD	Jennifer Anders, MD
2. Poisonings	Zachary Nayak, MD	Mitchell Goldstein, MD
	Jocelyn Ronda, MD	Suzanne Doyon, MD
3. Procedures	Bradley D. McCammack, MD	Jason Custer, MD
4. Trauma, Burns, and Common Critical Care Emergencies	Emily Krennerich, MD	Melissa J. Sacco, MD
		Dylan Stewart, MD
5. Adolescent Medicine	Natalie Spicyn, MD, MHS	Arik Marcell, MD, MPH
6. Analgesia and Procedural Sedation	Sean Barnes, MD, MBA	Myron Yaster, MD
7. Cardiology	Catherine B. Gretchen, MD	Jane Crosson, MD
	Arpana S. Rayannavar, MD	William Ravekes, MD
		W. Reid Thompson, MD
8. Dermatology	Jing Fang, MD	Bernard Cohen, MD
9. Development, Behavior, and Mental Health	Melissa Kwan, MD	Mary Leppert, MB, BCh, BAO
		Emily Frosch, MD
10. Endocrinology	Teresa Mark, MD	David Cooke, MD
11. Fluids and Electrolytes	Emily Young Thomas, MD	Michael Barone, MD
12. Gastroenterology	Tina Navidi, MD	Darla Shores, MD
13. Genetics: Metabolism and Dysmorphology	Jessica Duis, MD	Ronald Cohn, MD
		Ada Hamosh, MD
14. Hematology	Radha Gajjar, MD	James Casella, MD
	Elizabeth Jalazo, MD	Clifford Takemoto, MD
		Jeffrey Keffer, MD
15. Immunology and Allergy	Emily Braun, MD	Robert Wood, MD
16. Immunophylaxis	Jennifer Albon, MD	Ravit Boger, MD
17. Microbiology and Infectious Disease	Edith Dietz, MD	Pranita Tamma, MD
	Courtney Mangus, MD	
18. Neonatology	Lauren Beard, MD	Sue Aucott, MD
19. Nephrology	Katie Shaw, MD	Jeffrey Fadrowski, MD



<b>Chapter Title</b>	<b>Resident</b>	<b>Faculty Advisor</b>
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24. Pulmonology	Margaret Grala, MD	
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26. Rheumatology	Steven C. Marek, MD	
27. Blood Chemistries and Body Fluids	Branden Engorn, MD Jamie Flerlage, MD	
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30. Formulary Adjunct	Sara Mixter, MD, MPH J. Deanna Wilson, MD	Carlton K.K. Lee, PharmD, MPH
31. Drugs in Renal Failure	Monica C. Mix, MD Branden Engorn, MD	Carlton K.K. Lee, PharmD, MPH Angela Helder, PharmD

The Formulary, which is undoubtedly the most used handbook section, is complete, concise, and up to date thanks to the efforts of Carlton K.K. Lee, PharmD, MPH. With each edition, he carefully updates, revises, and improves the section. His herculean efforts make the Formulary one of the most useful and cited pediatric drug reference texts available.

We truly are humbled to have the opportunity to build on the great work of the preceding editors: Drs. Henry Seidel, Harrison Spencer, William Friedman, Robert Haslam, Jerry Winkelstein, Herbert Swick, Dennis Headings, Kenneth Schuberth, Basil Zitelli, Jeffery Biller, Andrew Yeager, Cynthia Cole, Peter Rowe, Mary Greene, Kevin Johnson, Michael Barone, George Siberry, Robert Iannone, Veronica Gunn, Christian Nechyba, Jason Robertson, Nicole Shilkofski, Jason Custer, Rachel Rau, Megan Tschudy, and Kristin Arcara. Many of these previous editors continue to contribute to the learning and maturation of the Harriet Lane house staff. They all are true examples of outstanding clinicians, educators, and mentors.

An undertaking of this magnitude could not have been accomplished without the support and dedication of some extraordinary people. First, a thanks to Kathy Miller, who has been an unwavering constant in the face of change, an advocate for residents, and a huge help with *The Harriet Lane Handbook*. We offer our deepest gratitude to our chairman, George Dover, whose compassion for children, dedication to improvement, and endless hours of service continue to enhance the Johns Hopkins Children's Center

and pediatric resident education. He has taught years of chief residents that "perfect is the evil of the good." Our special thanks go to our friends and mentors, Jeffrey Fadrowski and Barry Solomon, who have taught us that enthusiasm is a vector for change. Thank you to our program director, Janet Serwint, whose leadership continues to deeply enrich our lives. She is the example of excellence in patient care, scholarship, and education. Thank you for teaching us that "data is power." Finally, none of this would have been possible without Julia McMillan. She is a true academic pediatrician in every sense of the word. She is the consummate diagnostician who has shaped the careers of countless pediatricians. She will forever be the pediatrician we strive to emulate.

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Jessica Rubens  
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Shivang Shah  
Amena Smith  
Heather Wasik  
Olivia Widger

**Branden Engorn****Jamie Flerlage**

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# PART 1

## PEDIATRIC ACUTE CARE



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# Chapter 1

## Emergency Management

*Stephanie Chin-Sang, MD*

When approaching a patient in cardiopulmonary arrest, one must first and foremost focus on the A, B, C, D, and Es. The history, physical exam, and laboratory studies should closely follow a rapid primary assessment.

**NOTE:** The 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care updates the 2005 guidelines by recommending that immediate chest compressions should be the first step in reviving **victims of sudden cardiac arrest**, so the new acronym C-A-B has come into use and is presented in this section. The original A-B-C pathway remains the accepted method for rapid assessment and management of any critically ill patient.<sup>1</sup>

See the [2010 AHA CPR guidelines](#).

### I. INITIAL ASSESSMENT: C-A-B

**A. Assess pulse:** If infant/child is unresponsive and not breathing (gasps do not count as breathing), health care providers may take up to 10 seconds to feel for pulse (brachial in infant, carotid/femoral in child).<sup>2</sup>

1. **If pulseless**, immediately begin chest compressions (see [Circulation](#), B.1).
2. **If pulse**, begin A-B-C pathway of evaluation.

### II. AIRWAY<sup>3-6</sup>

#### A. Assessment

1. **Assess airway patency; think about obstruction:** Head tilt/chin lift (or jaw thrust if injury suspected) to open airway.
2. **Assess for spontaneous respiration:** If no spontaneous respirations, begin ventilating via rescue breaths, bag-mask, or endotracheal tube.
3. **Assess adequacy of respirations:**
  - a. Look for chest rise.
  - b. Recognize signs of distress (stridor, tachypnea, flaring, retractions, accessory muscle use, wheezes).

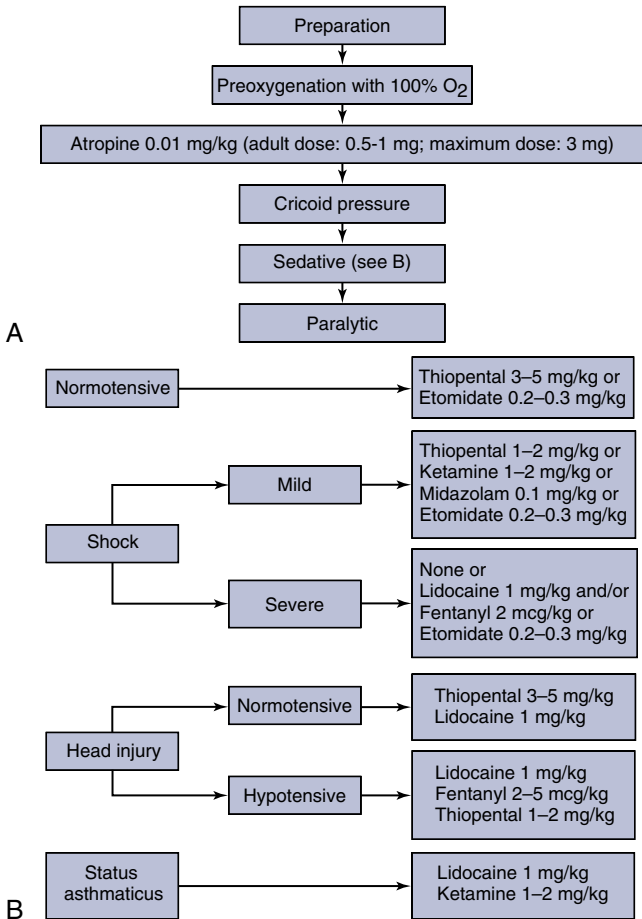
#### B. Management<sup>3-12</sup>

##### 1. Equipment

- a. Bag-mask ventilation with cricoid pressure may be used indefinitely if ventilating effectively (look at chest rise).
- b. Use oral or nasopharyngeal airway in patients with obstruction:
  - (1) Oral: Unconscious patients—measure from corner of mouth to mandibular angle.
  - (2) Nasal: Conscious patients—measure tip of nose to tragus of ear.

- c. Laryngeal mask airway (LMA): Simple way to secure an airway (no laryngoscopy needed), especially in difficult airways; does not prevent aspiration.
- 2. **Intubation:** Indicated for (impending) respiratory failure, obstruction, airway protection, pharmacotherapy, or need for likely prolonged support
  - a. Equipment (see page i): **SOAP** (**S**uction, **O**xygen, **A**irway Supplies, **P**harmacology)
    - (1) Laryngoscope blade:
      - (a) Miller (straight blade):
        - (i) #00-1 for premature to 2 months
        - (ii) #1 for 3 months to 3 years
        - (iii) #2 for > 3 years
      - (b) Macintosh (curved blade):
        - (i) #2 for > 2 years
        - (ii) #3 for > 8 years
    - (2) Endotracheal tube (ETT):
      - (a) Size determination: Internal diameter of ETT (mm) = (Age/4) + 4, or use length-based resuscitation tape to estimate.
      - (b) Approximate depth of insertion in cm = ETT size × 3.
      - (c) Uncuffed ETT for patients <8 years of age (note: cuffed tube can be used in children <8 y/o—see AHA guidelines for sizing recommendations).
      - (d) Stylet should not extend beyond the distal end of the ETT.
      - (e) Attach end-tidal CO<sub>2</sub> monitor as confirmation of placement and effectiveness of chest compressions if applicable.
    - (3) Nasogastric tube (NGT): To decompress the stomach; measure from nose to angle of jaw to xiphoid for depth of insertion.
  - b. Rapid sequence intubation (RSI) recommended for aspiration risk:
    - (1) Preoxygenate with non-rebreather at 100% O<sub>2</sub> for minimum of 3 minutes:
      - (a) Do not use positive-pressure ventilation (PPV) unless patient effort is inadequate.
      - (b) Children have less oxygen/respiratory reserve than adults, owing to higher oxygen consumption and lower functional residual capacity.
    - (2) See [Fig. 1-1](#) and [Table 1-1](#) for drugs used for RSI (adjunct, sedative, paralytic). Important considerations in choosing appropriate agents include clinical scenario, allergies, presence of neuromuscular disease, anatomic abnormalities, or hemodynamic status.
    - (3) For patients who are difficult to mask ventilate or have difficult airways, may consider sedation without paralysis and the assistance of subspecialists (anesthesiology and otolaryngology).
  - c. Procedure (attempts should not exceed 30 seconds):
    - (1) Preoxygenate with 100% O<sub>2</sub>.
    - (2) Administer intubation medications (see [Fig. 1-1](#) and [Table 1-1](#)).
    - (3) Apply cricoid pressure to prevent aspiration (Sellick maneuver) during bag-valve-mask ventilation and intubation. (Note: Use of cricoid pressure is optional; no benefit has been demonstrated.)



**FIGURE 1-1**

**A**, Treatment algorithm for intubation. **B**, Sedation options. (Modified from Nichols DG, Yaster M, Lappe DG, et al [eds]. *Golden Hour: The Handbook of Advanced Pediatric Life Support*. St Louis: Mosby; 1996:29.)

TABLE 1-1

## RAPID-SEQUENCE INTUBATION MEDICATIONS

Drug	Dose	Comments
<b>ADJUNCTS (FIRST)</b>		
Atropine (vagolytic)	0.01–0.02 mg/kg IV/IO Adult dose: 0.5–1.0 mg; max: 3 mg	+ Vagolytic; prevents bradycardia, especially with succinylcholine, and reduces oral secretions – Tachycardia, pupil dilation eliminates ability to examine pupillary reflexes Less than 0.1 mg may cause paradoxical bradycardia <b>Indication:</b> Can be used as premedication in all circumstances
Lidocaine (optional anesthetic)	1 mg/kg IV/IO; max 100 mg/dose	+ Blunts ICP spike, decreased gag/cough; controls ventricular arrhythmias <b>Indication:</b> Good premedication for shock, arrhythmia, elevated ICP, and status asthmaticus
<b>SEDATIVE-HYPNOTIC (SECOND)</b>		
Thiopental (barbiturate)	3–5 mg/kg IV/IO if normotensive 1–2 mg/kg IV/IO if hypotensive	+ Decreases O <sub>2</sub> consumption and cerebral blood flow – Vasodilation and myocardial depression; may increase oral secretions, cause bronchospasm/laryngospasm (not to be used in asthma) <b>Indication:</b> Drug of choice for increased ICP
Ketamine (NMDA receptor antagonist)	1–2 mg/kg IV/IO or 4–10 mg/kg IM	+ Bronchodilation; catecholamine release may benefit hemodynamically unstable patients – May increase BP, HR, and oral secretions; may cause laryngospasm; contraindicated in eye injuries; likely insignificant rise in ICP <b>Indication:</b> Drug of choice for asthma
Midazolam (benzodiazepine)	0.05–0.1 mg/kg IV/IO Max total dose of 10 mg	+ Amnestic and anticonvulsant properties – Respiratory depression/apnea, hypotension, and myocardial depression <b>Indication:</b> Mild shock
Fentanyl (opiate)	1–5 mcg/kg IV/IO <b>NOTE:</b> Fentanyl is dosed in mcg/kg, not mg/kg.	+ Fewest hemodynamic effects of all opiates – Chest wall rigidity with high dose or rapid administration; cannot use with MAOIs <b>Indication:</b> Shock
Etomidate (imidazole/hypnotic)	0.3 mg/kg IV/IO	+ Cardiovascular neutral; decreases ICP – Exacerbates adrenal insufficiency (inhibits 11-beta hydroxylase) <b>Indication:</b> Patients with severe shock, especially cardiac patients
Propofol (sedative-hypnotic)	2 mg/kg IV/IO	+ Extremely quick onset and short duration; blood pressure lowering; good antiemetic – Hypotension and profound myocardial depression; contraindicated in patients with egg allergy <b>Indication:</b> Induction agent for general anesthesia

TABLE 1-1

## RAPID-SEQUENCE INTUBATION MEDICATIONS (Continued)

Drug	Dose	Comments
<b>PARALYTICS (NEUROMUSCULAR BLOCKERS) (THIRD)</b>		
Succinylcholine (depolarizing)	1–2 mg/kg IV/IO 2–4 mg/kg IM	+ Quick onset (30–60 sec), short duration (3–6 min) make it an ideal paralytic – Irreversible; bradycardia in <5 years old or with rapid doses; increased risk of malignant hyperthermia; contraindicated in burns, massive trauma/muscle injury, neuromuscular disease, myopathies, eye injuries, renal insufficiency
Vecuronium (non-depolarizing)	0.1 mg/kg IV/IO	+ Onset 70–120 sec; cardiovascular neutral – Duration 30–90 min; must wait 30–45 min to reverse with glycopyrrolate and neostigmine <b>Indication:</b> When succinylcholine contraindicated or when longer-term paralysis desired
Rocuronium (non-depolarizing)	0.6–1.2 mg/kg IV/IO 1.8 mg/kg IM	+ Quicker onset (30–60 sec), shorter acting than vecuronium; cardiovascular neutral – Duration 30–60 min; may reverse in 30 min with glycopyrrolate and neostigmine

+, Potential advantages; –, potential disadvantages or cautions; BP, blood pressure; HR, heart rate; ICP, intracranial pressure; MAOI, monoamine oxidase inhibitor.

- (4) Use scissoring technique to open mouth.
- (5) Hold laryngoscope blade in left hand. Insert blade into right side of mouth, sweeping tongue to the left out of line of vision.
- (6) Advance blade to epiglottis. With straight blade, lift up, directly lifting the epiglottis to view cords. With curved blade, place tip in vallecula, elevate the epiglottis to visualize the vocal cords.
- (7) If possible, have another person hand over the tube, maintaining direct visualization, and pass through cords until black marker reaches the level of the cords.
- (8) Hold endotracheal tube firmly against the lip until tube is securely taped.
- (9) Verify ETT placement: observe chest wall movement, auscultation in both axillae and epigastrium, end-tidal CO<sub>2</sub> detection (there will be a false-negative response if there is no effective pulmonary circulation), improvement in oxygen saturation, chest radiograph, repeat direct laryngoscopy to visualize ETT.
- (10) If available, in-line continuous CO<sub>2</sub> detection should be used.

## III. BREATHING 3A, 3B, 3C

## A. Assessment

Once airway is secured, continually reevaluate ETT positioning (listen for breath sounds). Acute respiratory failure may signify **D**isplacement of the ETT, **O**bstruction, **P**neumothorax, or **E**quipment failure (DOPE).

## B. Management

1. **Mouth-to-mouth or mouth-to-nose breathing:** provide two slow breaths (1 sec/breath) initially. For newborns, apply one breath for every three chest compressions. In infants and children, apply two breaths after 30 compressions (one rescuer) or two breaths after 15 compressions (two rescuers). Breaths should have adequate volume to cause chest rise.
2. **Bag-mask ventilation** is used at a rate of 20 breaths/min (30 breaths/min in infants) using the E-C technique:
  - a. Use non-dominant hand to create a C with thumb and index finger over top of mask. Ensure a good seal, but *do not* push down on mask. Hook remaining fingers around the mandible (*not* the soft tissues of the neck!), with the fifth finger on the angle creating an E, and lift the mandible up toward the mask.
  - b. Assess chest expansion and breath sounds.
  - c. Decompress stomach with orogastric or nasogastric tube with prolonged bag-mask ventilation.
3. **Endotracheal intubation:** See prior section.

## IV. CIRCULATION<sup>3-5,13</sup>

### A. Assessment

1. **Rate/rhythm:** Assess for bradycardia, tachycardia, abnormal rhythm, or asystole. Generally, bradycardia requiring chest compressions is <60 beats/min; tachycardia of >220 beats/min suggests tachyarrhythmia rather than sinus tachycardia.
2. **Perfusion:**
  - a. Assess pulses, capillary refill (<2 sec = normal, 2 to 5 sec = delayed, >5 sec suggests shock), mentation, and urine output (if Foley in place).
  - b. If one cannot identify a pulse within 10 seconds, initiate cardiopulmonary resuscitation (CPR).
3. **Blood pressure (BP):** Hypotension is a late manifestation of circulatory compromise. Can be calculated in children >1 year with

formula: Hypotension = Systolic BP <  $[70 + (2 \times \text{Age in years})]$

### B. Management (Table 1-2)<sup>15</sup>

1. **Chest compressions**
  - a. Press hard ( $\frac{1}{3}$  to  $\frac{1}{2}$  anteroposterior [AP] diameter of chest) and fast (100-120 per minute) on backboard base with full recoil and minimal interruption.
  - b. Use end-tidal CO<sub>2</sub> to estimate effectiveness (<20 mmHg indicates inadequate compressions).
  - c. Use two-finger technique for infant if single rescuer available; otherwise, two thumbs with hands encircling chest is preferable.
2. **Use of automated external defibrillator (AED):** To determine whether rhythm is shockable, use an AED/defibrillator.

TABLE 1-2

## MANAGEMENT OF CIRCULATION

	Location*	Rate (per min)	Compressions: Ventilation
Infants	1 fingerbreadth below intermammary line	>100	15:2 (2 rescuers) 30:2 (1 rescuer)
Pre-pubertal children	2 fingerbreadths below intermammary line	≥100	15:2 (2 rescuers) 30:2 (1 rescuer)
Adolescents/adults	Lower half of sternum	100	30:2 (1 or 2 rescuers)

\*Depth of compressions should be one third to one half anteroposterior diameter of the chest.

### 3. Resuscitation with poor perfusion and shock:

- Optimize oxygen delivery with supplemental O<sub>2</sub>.
- Support respirations to reduce work of patient.
- Place intraosseous (IO) access immediately if in arrest and/or if intravenous (IV) access not obtained within 90 seconds.
- Resuscitation fluids are lactated Ringer's or normal saline.
  - Give up to three 20-mL/kg boluses each within 5 minutes for a total of 60 mL/kg in the first 15 minutes after presentation, checking for hepatomegaly after each bolus.
  - 5- to 10-mL/kg bolus in patient with cardiac insufficiency.
  - Consider colloid such as albumin, plasma, packed red blood cells (PRBCs) if poor response to crystalloids.
- Identify type of shock: Hypovolemia, cardiogenic (congenital heart disease, myocarditis, cardiomyopathy, arrhythmia), distributive (sepsis, anaphylaxis, neurogenic), obstructive (pulmonary embolus [PE], cardiac tamponade, tension pneumothorax).
- Pharmacotherapy (See inside front cover and consider stress-dose corticosteroids and/or antibiotics if applicable.)

## V. ALLERGIC EMERGENCIES (ANAPHYLAXIS) 18.17

### A. Definition

- A rapid-onset immunoglobulin (Ig) E-mediated systemic allergic reaction involving multiple organ systems, including two or more of the following:**
  - Cutaneous/mucosal** (flushing, urticaria, pruritus, angioedema); seen in 90%
  - Respiratory** (laryngeal edema, bronchospasm, dyspnea, wheezing, stridor, hypoxemia); seen in ≈70%
  - Gastrointestinal (GI)** (vomiting, diarrhea, nausea, crampy abdominal pain); seen in ≈ -40% to 50%
  - Circulatory** (tachycardia, hypotension, syncope); seen in ≈ -30% to 40%
- Initial reaction may be delayed for several hours AND symptoms may recur up to 72 hours after initial recovery.** Patients should therefore be observed for a minimum of 6 to 24 hours for late-phase symptoms.

### B. Initial Management

- Remove/stop exposure to precipitating antigen.**

2. **Epinephrine** = mainstay of therapy. While performing ABCs, immediately give intramuscular (IM) epinephrine, 0.01 mg/kg (0.01 mL/kg) of 1:1000 subcutaneously (SQ) or IM (maximum dose 0.5 mg). Repeat every 5 minutes as needed. Site of choice is lateral aspect of the thigh, owing to its vascularity.
3. **Establish airway** and give O<sub>2</sub> and PPV as needed.
4. **Obtain IV access**, Trendelenburg position with head 30 degrees below feet, administer fluid boluses followed by pressors as needed.
5. **Histamine-1 receptor antagonist** such as diphenhydramine, 1 to 2 mg/kg via IM, IV, or oral (PO) route (maximum dose, 50 mg). Also consider a histamine-2 receptor antagonist (e.g., ranitidine).
6. **Corticosteroids** help prevent the late phase of the allergic response. Administer methylprednisolone in a 2-mg/kg IV bolus, followed by 2 mg/kg/day IV or IM, divided every 6 hours, or prednisone, 2 mg/kg PO once daily.
7. **Albuterol** 2.5 mg for <30 kg, 5 mg for >30 kg, for bronchospasm or wheezing. Repeat every 15 minutes as needed.
8. **Racemic epinephrine** 0.5 mL of 2.25% solution inhaled for signs of upper airway obstruction
9. Patient should be discharged with an **Epi-Pen** (>30 kg), **Epi-Pen Junior** (<30 kg), or comparable injectable epinephrine product with specific instructions on appropriate use, as well as an anaphylaxis action plan.

## VI. RESPIRATORY EMERGENCIES

The hallmark of upper airway obstruction is stridor, whereas lower airway obstruction is characterized by cough, wheeze, and a prolonged expiratory phase.

### A. Asthma<sup>19,20</sup>

Lower airway obstruction resulting from triad of inflammation, bronchospasm, and increased secretions:

1. **Assessment:** Respiratory rate (RR), work of breathing, O<sub>2</sub> saturation, heart rate (HR), peak expiratory flow, alertness, color
2. **Initial management:**
  - a. Give O<sub>2</sub> to keep saturation >95%.
  - b. Administer inhaled  $\beta$ -agonists: Nebulized albuterol as often as needed.
  - c. Ipratropium bromide
  - d. Steroids: Methylprednisolone, 2 mg/kg IV/IM bolus, then 2 mg/kg/day divided every 6 hours; *or* prednisone/prednisolone, 2 mg/kg PO every 24 hours; requires minimum of 3 to 4 hours to take effect.
  - e. If air movement is still poor despite maximizing above therapy:
    - (1) Epinephrine: 0.01 mg/kg (0.01 mL/kg) of 1:1000 subcutaneously (SQ) or IM (maximum dose 0.5 mg)
      - (a) Bronchodilator, vasopressor, and inotropic effects
      - (b) Short-acting (~15 min) and should be used as temporizing rather than definitive therapy



- (2) Magnesium sulfate: 25 to 75 mg/kg/dose IV or IM (maximum 2 g) infused over 20 minutes.
  - (a) Smooth muscle relaxant; relieves bronchospasm.
  - (b) Many clinicians advise giving a saline bolus prior to administration, because hypotension may result.
  - (c) Contraindicated if patient already has significant hypotension or renal insufficiency.
- (3) Terbutaline: 0.01 mg/kg SQ (maximum dose 0.4 mg) every 15 minutes up to three doses.
  - (a) Systemic  $\beta_2$ -agonist limited by cardiac intolerance.
  - (b) Monitor continuous 12-lead electrocardiogram (ECG), cardiac enzymes, urinalysis (UA), and electrolytes.

3. **Further management:** If incomplete or poor response, consider obtaining an arterial blood gas value.

**NOTE:** A normalizing  $P_{CO_2}$  is often a sign of impending respiratory failure.

- a. Maximize and continue initial treatments.
- b. Terbutaline 2 to 10 mcg/kg IV load, followed by continuous infusion of 0.1 to 4 mcg/kg/min titrated to effect in increments of 0.1 to 0.2 mcg/kg/min every 30 minutes depending on clinical response. Infusion should be started with lowest possible dose; doses as high as 10 mcg/kg/min have been used. Use appropriate cardiac monitoring in intensive care unit (ICU), as above.
- c. A helium ( $\geq 70\%$ ) and oxygen mixture may be of some benefit in the critically ill patient but is more useful in upper airway edema. Avoid use in the hypoxic patient.
- d. Methylxanthines (e.g., aminophylline) may be considered in the ICU setting but have significant side effects and have not been shown to affect intubation rates or length of hospital stay.
- e. Noninvasive positive-pressure ventilation (e.g., BiPAP) may be used in patients with impending respiratory failure, both as a temporizing measure and to avoid intubation, but requires a cooperative patient with spontaneous respirations.
4. **Intubation** of those with acute asthma is dangerous and should be reserved for impending respiratory arrest.
  - a. Indications for endotracheal intubation include deteriorating mental status, severe hypoxemia, and respiratory or cardiac arrest.
  - b. Use lidocaine as adjunct and ketamine for sedative (see [Fig. 1-1](#) and [Table 1-1](#)).
  - c. Consider using an inhaled anesthetic such as isoflurane.
5. **Hypotension:** Result of air trapping, hyperinflation, and therefore decreased pulmonary venous return. See [Section IV.B.3](#) for management. Definitive treatment is reducing lower airway obstruction.

## B. Upper Airway Obstruction<sup>21-24</sup>

Upper airway obstruction is most commonly caused by foreign-body aspiration or infection.

1. **Epiglottitis:** Most often affects children between 2 and 7 years, but may occur at any age. This is a true emergency involving cellulitis and edema of the epiglottis, aryepiglottic folds, and hypopharynx.
  - a. Patient is usually febrile, anxious, and toxic appearing, with sore throat, drooling, respiratory distress, stridor, tachypnea, and *tripod positioning* (sitting forward supported by both arms, with neck extended and chin thrust out). Any agitation of the child may cause complete obstruction, so avoid invasive procedures/evaluation until airway is secured.
  - b. Unobtrusively give O<sub>2</sub> (blow-by). Nothing by mouth, monitor with pulse oximetry, allow parent to hold patient.
  - c. Summon epiglottitis team (most senior pediatrician, anesthesiologist, intensive care physician, and otolaryngologist in hospital).
  - d. Management options:
    - (1) If unstable (unresponsive, cyanotic, bradycardic) → emergently intubate.
    - (2) If stable with high suspicion → take patient to operating room for laryngoscopy and intubation under general anesthesia.
    - (3) If stable with moderate or low suspicion → obtain lateral neck radiographs to confirm.
  - e. After airway is secure, obtain cultures of blood and epiglottic surface. Begin antibiotics to cover *Haemophilus influenzae* type B, *Streptococcus pneumoniae*, group A streptococci, *Staphylococcus aureus*.
  - f. Epiglottitis may also be caused by thermal injury, caustic ingestion, or foreign body.
2. **Croup (laryngotracheobronchitis):** Most common in infants 6 to 36 months. Croup is a common syndrome involving inflammation of the subglottic area; presents with fever, barking cough, and stridor. Patients rarely appear toxic, as in epiglottitis.
  - a. Mild (no stridor at rest): Treat with minimal disturbance, cool mist, hydration, antipyretics, and consider steroids.
  - b. Moderate to severe:
    - (1) The efficacy of mist therapy is not established.
    - (2) Racemic epinephrine. After administering, observe for a minimum of 2 to 4 hours, owing to potential for rebound obstruction. Hospitalize if more than one nebulization required.
    - (3) Dexamethasone, 0.3 to 0.6 mg/kg IV, IM, or PO once. Effect lasts 2 to 3 days. Alternatively, nebulized budesonide (2 mg) may be used, though little data exist to support its use, and some studies find it inferior to dexamethasone.
    - (4) A helium-oxygen mixture may decrease resistance to turbulent gas flow through a narrowed airway.
  - c. If a child fails to respond as expected to therapy, consider other etiologies (e.g., retropharyngeal abscess, bacterial tracheitis, subglottic stenosis, epiglottitis, foreign body). Obtain airway radiography, computed tomography (CT), and evaluation by otolaryngology or anesthesiology.

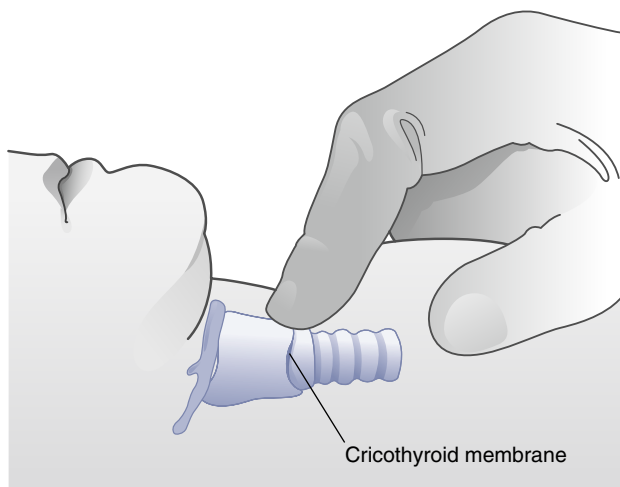


3. **Foreign-body aspiration:** Occurs most often in children 6 months to 3 years old. It frequently involves hot dogs, candy, peanuts, grapes, or balloons. Most events unwitnessed, so suspect this in children with sudden-onset choking, stridor, or wheezing.
- a. If the patient is stable (i.e., forcefully coughing, well oxygenated), removal of the foreign body by bronchoscopy or laryngoscopy should be attempted in a controlled environment.
  - b. If the patient is unable to speak, moves air poorly, or is cyanotic:
    - (1) Infant: Place infant over arm or rest on lap. Give five back blows between the scapulae. If unsuccessful, turn infant over and give five chest thrusts (*not* abdominal thrusts).
    - (2) Child: Perform five abdominal thrusts (Heimlich maneuver) from behind a sitting or standing child.
    - (3) After back, chest, and/or abdominal thrusts, open mouth using tongue-jaw lift and remove foreign body if visualized. Do not attempt blind finger sweeps. Magill forceps may be used to retrieve objects in the posterior pharynx. Ventilate if unconscious, and repeat sequence as needed.
    - (4) If there is complete airway obstruction and the patient cannot be ventilated by bag-valve mask or ETT, consider percutaneous (needle) cricothyrotomy (Fig. 1-2).<sup>4</sup>

## VII. NEUROLOGIC EMERGENCIES

### A. Altered States of Consciousness<sup>25</sup>

- 1. **Assessment:** Range of mental status includes alert, confused, disoriented, delirious, lethargic, stuporous, and comatose.
  - a. History: Consider structural versus medical causes (Box 1-1). Obtain history of trauma, ingestion, infection, fasting, drug use, diabetes, seizure, or other neurologic disorder.
  - b. Examination: Assess HR, BP, respiratory pattern, Glasgow Coma Scale (Table 1-3), temperature, pupillary response, funduscopy (a late finding, absence of papilledema does not rule out increased intracranial pressure [ICP]), rash, abnormal posturing, and focal neurologic signs.
2. **Acute traumatic head injury:**<sup>26</sup>
- a. Assess pupillary response:
    - (1) Blown pupil: Elevate head of bed, hyperventilate, maintain blood pressure, administer hypertonic saline and/or mannitol.
3. **Management of coma:**
- a. **A**irway (with cervical spine immobilization), **B**reathing, **C**irculation, **D**-stick, **O**xxygen, **N**aloxone, **T**hiamine (ABC DON'T)
    - (1) Naloxone, 0.1 mg/kg IV, IM, SQ, or ETT (maximum dose, 2 mg). Repeat as necessary, given short half-life (in case of opiate intoxication).
    - (2) Thiamine, 100 mg IV (before starting glucose in adolescents, in case of alcoholism or eating disorder).
    - (3) D<sub>25</sub>W, 2 to 4 mL/kg IV bolus if hypoglycemia is present.

**FIGURE 1-2**

Percutaneous (needle) cricothyrotomy. Extend neck, attach a 3-mL syringe to a 14- to 18-gauge intravenous catheter, and introduce catheter through cricothyroid membrane (inferior to thyroid cartilage, superior to cricoid cartilage). Aspirate air to confirm position. Remove syringe and needle, attach catheter to an adaptor from a 3.0-mm endotracheal tube, which can then be used for positive-pressure oxygenation. (*Modified from Dieckmann RA, Fiser DH, Selbst SM. Illustrated Textbook of Pediatric Emergency and Critical Care Procedures. St Louis: Mosby, 1997:118.*)

**BOX 1-1****DIFFERENTIAL DIAGNOSIS OF ALTERED LEVEL OF CONSCIOUSNESS****I. STRUCTURAL CAUSES**

Vascular—e.g., cerebrovascular accident, cerebral vein thrombosis

Increased intracranial pressure—e.g., hydrocephalus, tumor, abscess, cyst, subdural empyema, pseudotumor cerebri

Trauma (intracranial hemorrhage, diffuse cerebral swelling, shaken baby syndrome)

**II. MEDICAL CAUSES**

Anoxia

Hypothermia/hyperthermia

Metabolic—e.g., inborn errors of metabolism, diabetic ketoacidosis, hyperammonemia, uremia, hypoglycemia, electrolyte abnormality

Infection—e.g., sepsis, meningitis, encephalitis, subdural empyema

Seizure/postictal state

Toxins/ingestions

Psychiatric/psychogenic

TABLE 1-3

## COMA SCALES

Glasgow Coma Scale		Modified Coma Scale for Infants	
Activity	Best Response	Activity	Best Response
<b>EYE OPENING</b>			
Spontaneous	4	Spontaneous	4
To speech	3	To speech	3
To pain	2	To pain	2
None	1	None	1
<b>VERBAL</b>			
Oriented	5	Coo/babbles	5
Confused	4	Irritable	4
Inappropriate words	3	Cries to pain	3
Nonspecific sounds	2	Moans to pain	2
None	1	None	1
<b>MOTOR</b>			
Follows commands	6	Normal spontaneous movements	6
Localizes pain	5	Withdraws to touch	5
Withdraws to pain	4	Withdraws to pain	4
Abnormal flexion	3	Abnormal flexion	3
Abnormal extension	2	Abnormal extension	2
None	1	None	1

Data from Jennet B, Teasdale G. Aspects of coma after severe head injury. *Lancet*. 1977;1:878; and James HE. Neurologic evaluation and support in the child with an acute brain insult. *Pediatr Ann*. 1986;15:16.

- Laboratory tests: Consider complete blood cell count (CBC), electrolytes, liver function tests,  $\text{NH}_3$ , lactate, toxicology screen (serum and urine; always include salicylate and acetaminophen levels), blood gas, serum osmolality, prothrombin time (PT)/partial thromboplastin time (PTT), and blood/urine culture. If patient is an infant or toddler, consider assessment of plasma amino acids, urine organic acids, and other appropriate metabolic workup.
- If meningitis or encephalitis is suspected, consider lumbar puncture (LP) and start antibiotics and acyclovir.
- Request emergency head CT after ABCs are stabilized; consider neurosurgical consultation and electroencephalogram (EEG) if indicated.
- If ingestion is suspected, airway must be protected before GI decontamination (see Chapter 2).
- Monitor Glasgow Coma Scale and reassess frequently (see Table 1-3).

## B. Status Epilepticus<sup>27,28</sup>

See Chapter 20 for non-acute evaluation and management of seizures.

- Assessment:** Common causes of childhood seizures include electrolyte abnormalities, hypoglycemia, fever, subtherapeutic anticonvulsant levels, central nervous system (CNS) infections, trauma, toxic ingestion, and metabolic abnormalities. Consider specific patient history, such as

shunt malfunction in patient with ventriculoperitoneal shunt. Less common causes include vascular, neoplastic, and endocrine diseases.

2. **Acute management of seizures** (Table 1-4): If CNS infection is suspected, give antibiotics and/or acyclovir early.
3. **Diagnostic workup:** When stable, workup may include CT or magnetic resonance imaging, EEG, and LP.

TABLE 1-4

## ACUTE MANAGEMENT OF SEIZURES

Time (min)	Intervention
0–5	Stabilize patient. Assess airway, breathing, circulation, and vital signs. Administer oxygen. Obtain IV or IO access. Consider hypoglycemia, thiamine deficiency, intoxication (dextrose, thiamine, naloxone may be given immediately if suspected). Obtain laboratory studies: consider glucose, electrolytes, calcium, magnesium, blood gas, CBC, BUN, creatinine, LFTs, toxicology screen, anticonvulsant levels, blood culture (if infection is suspected). Initial screening history and physical examination
5–15	Begin pharmacotherapy: Lorazepam (Ativan), 0.05–0.1 mg/kg IV/IM, max dose 2 mg Or Diazepam (Valium), 0.2–0.5 mg/kg IV (0.5 mg/kg rectally); max dose <5 y/o: 5 mg, >5 y/o: 10 mg May repeat lorazepam or diazepam 5–10 min after initial dose
15–25	If seizure persists, load with one of the following: <ol style="list-style-type: none"> <li>1. Fosphenytoin* 15–20 mg PE/kg IV/IM at 3 mg PE/kg/min via peripheral IV line (maximum 150 mg PE/min). If given IM, may require multiple dosing sites.</li> <li>2. Phenytoin† 15–20 mg/kg IV at rate not to exceed 1 mg/kg/min via central line</li> <li>3. Phenobarbital 15–20 mg/kg IV at rate not to exceed 1 mg/kg/min</li> </ol>
25–40	If seizure persists: Levetiracetam 20–30 mg/kg IV at 5 mg/kg/min; or valproate 20 mg/kg IV at 5 mg/kg/min May give phenobarbital at this time if still seizing at 5 minutes and (fos) phenytoin previously used Additional phenytoin or fosphenytoin 5 mg/kg over 12 hr for goal serum level of 10 mg/L Additional phenobarbital 5 mg/kg/dose every 15–30 min (maximum total dose of 30 mg/kg; be prepared to support respirations)
40–60	If seizure persists,‡ consider pentobarbital, midazolam, or general anesthesia in intensive care unit. Avoid paralytics.

\*Fosphenytoin dosed as phenytoin equivalent (PE).

†Phenytoin may be contraindicated for seizures secondary to alcohol withdrawal or most ingestions (see Chapter 2).

‡Pyridoxine 100 mg IV in infant with persistent initial seizure.

BUN, Blood urea nitrogen; CBC, complete blood cell count; CT, computed tomography; EEG, electroencephalogram; LFTs, liver function tests; IM, intramuscular; IO, intraosseous; IV, intravenous.

Modified from Abend, NS, Dlugos, DJ. Treatment of refractory status epilepticus: literature review and a proposed protocol. *Pediatr Neurol*. 2008;38:377.

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# Chapter 2

## Poisonings

Zachary Nayak, MD, and Jocelyn Ronda, MD

2

 See additional content on Expert Consult

### I. WEBSITES

American Association of Poison Control Centers: <http://www.aapcc.org/dnn/Home.aspx>

American Academy of Clinical Toxicology: <http://www.clintox.org/index.cfm>  
Centers for Disease Control and Prevention, Section on Environmental Health: <http://www.cdc.gov/Environmental/>

### II. INITIAL EVALUATION

#### A. History

##### 1. Exposure history

- Obtain history from witnesses and/or close contacts.
- Route, timing, and number of exposures (acute, chronic, or repeated ingestion), prior treatments or decontamination efforts.<sup>1,2</sup>

##### 2. Substance identification

- Attempt to identify exact name of substance ingested and constituents, including product name, active ingredients, possible contaminants, expiration date, concentration, and dose.
- Consult local poison control for pill identification: 1-800-222-1222.

##### 3. Quantity of substance ingested

- Attempt to estimate a missing volume of liquid or the number of missing pills from a container.

##### 4. Environmental information

- Accessible items in the house or garage; open containers; spilled tablets; household members taking medications, herbs, or other complementary medicines.<sup>2</sup>

#### B. Laboratory Findings

- Toxicology screens:** Includes amphetamines, barbiturates, cocaine, ethanol, and opiates (Table 2-1).

- If a particular type of ingestion is suspected, verify that the agent is included in the toxicology test.<sup>2</sup>
- When obtaining a urine toxicology test, consider measuring both aspirin and acetaminophen blood levels because these are common analgesic ingredients in many medications.<sup>2</sup>
- Gas chromatography or gas mass spectroscopy can distinguish medications that may cause a false-positive toxicology screen.<sup>3</sup>

**TABLE 2-1**  
**URINE TOXICOLOGY SCREEN\***

Agent	Time Detectable in Urine
Amphetamines	2–4 days; up to 15 days
Benzodiazepines	3 days (if short-term use); 4–6 weeks (if >1 year use)
Buprenorphine	3–4 days
Cannabinoids	2–7 days (occasional use); 21–30 days (chronic use)
Cocaine	12 hours (parent form); 12–72 hours (metabolites)
Codeine	2–6 days
Ethanol	2–4 hours; up to 24 hours
Heroin	2–4 days
Hydromorphone	2–4 days
Methadone	Up to 3 days
Methamphetamine	2–5 days (depends on urine pH)
Morphine	2–4 days (up to 14 days)
Phencyclidine (PCP)	2–8 days (occasional use); 30 days (regular use)

\*Recognize drugs not detected by routine toxicology screens.  
The length of detection of drugs of abuse in urine varies. The above periods of detection should only be considered rough estimates and depend upon the individual's metabolism, physical condition, fluid intake, frequency, and quantity of ingestion.<sup>4</sup>

**C. Clinical Diagnostic Aids (Table EC 2-A)**

**III. TOXIDROMES (TABLE 2-2)**

**TABLE 2-2**  
**TOXIDROMES**

Drug Class	Signs and Symptoms	Causative Agents
<b>Anticholinergic:</b> "Mad as a hatter, red as a beet, blind as a bat, hot as a hare, dry as a bone."	Delirium, psychosis, paranoia, dilated pupils, thirst, hyperthermia, ↑HR, urinary retention	Antihistamines, phenothiazines, scopolamine, tricyclic antidepressants
<b>Cholinergic: Muscarinic</b>	Salivation, lacrimation, urination, defecation, ↑HR, emesis, bronchospasm	Organophosphates
<b>Cholinergic: Nicotinic</b>	Muscle fasciculations, paralysis, ↑HR, ↑BP	Tobacco, black widow venom, insecticides
<b>Opiates</b>	Sedation, constricted pupils, hypoventilation, ↓BP	Opioids
<b>Sympathomimetics</b>	Agitation, dilated pupils, ↑HR, ↓BP, moist skin	Amphetamines, cocaine, albuterol, caffeine, PCP
<b>Sedative/hypnotic</b>	Depressed mental status, normal pupils, ↓BP	Benzodiazepines, barbiturates,
<b>Serotonergic</b>	Confusion, flushing, ↑HR, shivering, hyperreflexia, muscle rigidity, clonus	SSRIs (alone or in combination with other meds including MAOIs, tramadol, and TCAs)



TABLE EC2-A

## CLINICAL DIAGNOSTIC AIDS

Clinical Sign	Intoxicant
<b>VITAL SIGNS</b>	
Hypothermia	Alcohol, antidepressants, barbiturates, carbamazepine, carbon monoxide, clonidine, ethanol, hypoglycemics, opioids, phenothiazines, sedative-hypnotics
Hyperpyrexia	Amphetamines, anticholinergics, antihistamines, atropinics, $\beta$ -blockers, cocaine, iron, isoniazid, monoamine oxidase inhibitors (MAOIs), phencyclidine, phenothiazines, quinine, salicylates, sympathomimetics, selective serotonin reuptake inhibitors (SSRIs), theophylline, thyroxine, tricyclic antidepressants (TCAs)
Bradypnea	Acetone, alcohol, barbiturates, botulinum toxin, clonidine, ethanol, ibuprofen, opioids, nicotine, sedative-hypnotics
Tachypnea	Amphetamines, barbiturates, carbon monoxide, cyanide, ethylene glycol, isopropanol, methanol, salicylates <i>Direct pulmonary insult:</i> hydrocarbons, organophosphates, salicylates
Bradycardia	$\alpha$ -Agonists, alcohols, $\beta$ -blockers, calcium channel blockers, central $\alpha_2$ -agonist, clonidine, cyanide, digoxin, opioids, organophosphates, plants (lily of the valley, foxglove, oleander), sedative-hypnotics
Tachycardia	Alcohol, amphetamines, anticholinergics, antihistamines, atropine, cocaine, cyclic antidepressants, cyanide, iron, phencyclidine, salicylates, sympathomimetics, theophylline, TCAs, thyroxine
Hypotension	$\alpha$ -Agonists, angiotensin-converting enzyme (ACE) inhibitors, barbiturates, carbon monoxide, cyanide, iron, methemoglobinemia, opioids, phenothiazine, sedative-hypnotics, TCAs <i>Profound hypotension:</i> $\beta$ -blockers, calcium channel blockers, clonidine, cyclic antidepressants, digoxin, imidazolines, nitrites, quinidine, propoxyphene, theophylline
Hypertension	Amphetamines, anticholinergics, antihistamines, atropinics, clonidine, cocaine, cyclic antidepressants (early after ingestion), diet pills, ephedrine, MAOIs, nicotine, over-the-counter cold remedies, phencyclidine, phenylpropylamine, pressors, sympathomimetics, TCAs <i>Delayed hypertension:</i> Thyroxine
Hypoxia	Oxidizing agents

## NEUROMUSCULAR

Nervous system instability	<i>Insidious onset:</i> Acetaminophen, benzocaine, opioids <i>Abrupt onset:</i> Lidocaine, monocyclic or tricyclic antidepressants, phenothiazines, theophylline <i>Delayed onset:</i> Atropine, diphenoxylate <i>Transient instability:</i> Hydrocarbons
Depression and excitation	Clonidine, imidazolines, phencyclidine
Ataxia	Alcohol, anticonvulsants, barbiturates, carbon monoxide, heavy metals, hydrocarbons, solvents, sedative-hypnotics
Chvostek/Trousseau signs	Ethylene glycol, hydrofluoric acid-induced hypocalcemia, phosphate-induced hypocalcemia from Fleet enema

Continued

TABLE EC2-A—cont'd

Clinical Sign	Intoxicant
Coma	Alcohol, anesthetics, anticholinergics (antihistamines, antidepressants, phenothiazines, atropinics, over-the-counter sleep preparations), anticonvulsants, baclofen, barbiturates, benzodiazepines, bromide, carbon monoxide, chloral hydrate, clonidine, cyanide, cyclic antidepressants, $\gamma$ -hydroxybutyrate (GHB), hydrocarbons, hypoglycemics, inhalants, insulin, lithium, opioids, organophosphate insecticides, phenothiazines, salicylates, sedative-hypnotics, tetrahydrozoline, theophylline
Delirium, psychosis	Alcohol, anticholinergics (including cold remedies), cocaine, heavy metals, heroin, LSD, marijuana, mescaline, methaqualone, peyote, phencyclidine, phenothiazines, steroids, sympathomimetics
Miosis	Barbiturates, clonidine, ethanol, opioids, organophosphates, phencyclidine, phenothiazines, muscarinic mushrooms
Mydriasis	Amphetamines, antidepressants, antihistamines, atropinics, barbiturates (if comatose), botulism, cocaine, glutethimide, LSD, marijuana, methanol, phencyclidine
Nystagmus	Barbiturates, carbamazepine, diphenylhydantoin, ethanol, glutethimide, MAOIs, phencyclidine (both vertical and horizontal), sedative-hypnotics
Paralysis	Botulism, heavy metals, paralytic shellfish poisoning, plants (poison hemlock)
Seizures	Ammonium fluoride, amphetamines, anticholinergics, antidepressants, antihistamines, atropine, $\beta$ -blockers, boric acid, bupropion, caffeine, camphor, carbamates, carbamazepine, carbon monoxide, chlorinated insecticides, cocaine, cyclic antidepressants, diethyltoluamide, ergotamine, ethanol, GHB, <i>Gyromitra</i> mushrooms, hydrocarbons, hypoglycemics, ibuprofen, imidazolines, isoniazid, lead, lidocaine, lindane, lithium, LSD, meperidine, nicotine, opioids, organophosphate insecticides, phencyclidine, phenothiazines, phenylpropanolamine, phenytoin physostigmine, plants (water hemlock), propoxyphene, salicylates, strychnine, theophylline

**CARDIOVASCULAR**

Hypoperfusion	Calcium channel blockers, iron
Wide QRS complex	TCAs

**ELECTROLYTES**

Anion gap metabolic acidosis	Acetaminophen, carbon monoxide, chronic toluene, cyanide, ethylene glycol, ibuprofen, iron, isoniazid, lactate, methanol, metformin, paraldehyde, phenformin, salicylates
Electrolyte disturbances	Diuretics, salicylates, theophylline
Hypoglycemia	Alcohol, $\beta$ -blockers, hypoglycemics, insulin, salicylates
Serum osmolar gap	Acetone, ethanol, ethylene glycol, isopropyl alcohol, methanol, propylene glycol Calculated osmolarity = $(2 \times \text{serum Na}) + \text{BUN}/2.8 + \text{glucose}/18$ . Normal osmolarity is 290 mOsm/kg

**SKIN**

Asymptomatic cyanosis	Methemoglobinemia
Cyanosis unresponsive to oxygen	Aniline dyes, benzocaine, nitrites, nitrobenzene, phenazopyridine, phenacetin
Flushing	Alcohol, antihistamines, atropinics, boric acid, carbon monoxide, cyanide, disulfiram

TABLE EC2-A—cont'd

Clinical Sign	Intoxicant
Jaundice	Acetaminophen, carbon tetrachloride, heavy metals (iron, phosphorus, arsenic), naphthalene, phenothiazines, plants (mushrooms, fava beans)
<b>ODORS</b>	
Acetone	Acetone, isopropyl alcohol, phenol, salicylates
Alcohol	Ethanol
Bitter almond	Cyanide
Garlic	Heavy metal (arsenic, phosphorus, thallium), organophosphates
Hydrocarbons	Hydrocarbons (gasoline, turpentine, etc.)
Oil of wintergreen	Salicylates
Pear	Chloral hydrate
Violets	Turpentine
<b>RADIOLOGY</b>	
Small opacities on radiograph	Halogenated toxins, heavy metals, iron, lithium, densely packaged products

## IV. INGESTION AND ANTIDOTES (TABLE 2-3)

**A. In general, the following are guidelines of supportive care for the management of ingestions.**

1. **For hypotension**, patients often require aggressive fluid resuscitation or vasopressors.
2. **Treat hyperpyrexia with cooling measures.**
3. **For ingestions that cause seizure**, treat with benzodiazepines unless otherwise specified.
4. **Selective decontamination with activated charcoal.**
5. **Hemodialysis** may be indicated to remove a drug/toxin regardless of renal function or in cases of renal impairment.

**B. Consult local poison control for further management at 1-800-222-1222. Consult Poisindex if available.**

TABLE 2-3

COMMONLY INGESTED AGENTS<sup>4</sup>

Ingested Agent	Signs and Symptoms	Antidote <sup>4</sup>
Acetaminophen	See Section V	
Amphetamine	See sympathomimetics toxidrome in Table 2-3	Supportive care (see above)
Anticholinergics <sup>1</sup>	See anticholinergic toxidrome in Table 2-3	<b>Physostigmine:</b> See formulary for dosing
Anticholinesterase (insecticides, donepezil, mushrooms)	See cholinergic: muscarinic and cholinergic: nicotinic toxidrome in Table 2-3	<b>Atropine:</b> See formulary for dosing
Antihistamines <sup>5</sup>	See anticholinergic toxidrome in Table 2-3; paradoxical CNS stimulation, dizziness, seizures	Supportive care (see above)
Benzodiazepines <sup>6,7</sup>	Coma, dysarthria, ataxia, drowsiness, hallucinations, confusion, agitation, bradycardia, hypotension, respiratory depression	<b>Flumazenil:</b> See formulary for dosing
$\beta$ -blockers <sup>8-10</sup>	Coma, seizures, altered mental status, hallucinations, bradycardia, congestive heart failure, hypotension, respiratory depression, bronchospasm, hypoglycemia	<b>Glucagon:</b> See formulary for dosing; see <b>insulin/dextrose</b> treatment in calcium channel blockers
Calcium channel blockers <sup>9,10</sup>	Seizures, coma, dysarthria, lethargy, confusion, cardiac arrhythmia, hypotension, pulmonary edema, hyperglycemia, flushing	<b>CaCl (10%):</b> See formulary for dosing <b>CaGluc (10%):</b> See formulary for dosing <b>Glucagon:</b> See formulary for dosing <b>Insulin/dextrose:</b> 1 U/kg bolus $\rightarrow$ infuse at 0.1–1 U/kg/hr; give with D25% 0.25 g/kg bolus $\rightarrow$ 0.5 g/kg/hr infusion

Continued

TABLE 2-3—cont'd

Ingested Agent	Signs and Symptoms	Antidote <sup>4</sup>
Clonidine <sup>10</sup>	Symptoms resemble an opioid toxidrome. CNS depression, coma, lethargy, hypothermia, miosis, bradycardia, profound hypotension, respiratory depression	See opioid antidote
Cocaine <sup>11</sup>	See sympathomimetics toxidrome in Table 2-3	Supportive care (see above)
Ecstasy <sup>11</sup>	Hallucinations, teeth grinding, hyperthermia, seizures	Supportive care (see above)
Ethanol <sup>1,12</sup>	See sedative/hypnotic toxidrome in Table 2-3	Supportive care (see above)
Ethylene glycol/methanol <sup>1,12</sup>	Similar to ethanol; additionally blurry or double vision, metabolic acidosis, abdominal pain	<b>Fomepizole:</b> See formulary for dosing. Alternatively, if not available, can use Ethanol (see formulary for dosing), but requires more monitoring than fomepizole.
Iron <sup>13,14</sup>	Vomiting, diarrhea, IBP, lethargy, renal failure	<b>Deferoxamine:</b> See formulary for dosing
Lead	See Section VI	
NSAIDs	Nausea, vomiting, epigastric pain, headache, GI hemorrhage, renal failure	Supportive care (see above)
Opioids	See opioid toxidrome in Table 2-3	<b>Naloxone:</b> See formulary for dosing
Organophosphates	See cholinergic/muscarinic toxidrome in Table 2-3	If muscle fasciculations, respiratory depression, coma, use <b>Pralidoxime:</b> see formulary for dosing. <b>Atropine:</b> used for muscarinic effects (see anticholinesterase)
Salicylates <sup>12</sup>	GI upset, tinnitus, tachypnea, hyperpyrexia, dizziness, lethargy, dysarthria, seizure, coma, cerebral edema	Supportive care (see above)
Serotonin syndrome	Seizures, muscle rigidity, myoclonus, hyperpyrexia, flushing, rhabdomyolysis	<b>Cyproheptadine:</b> See formulary for dosing; <i>for agitation:</i> <b>Diazepam:</b> See formulary for dosing
Sulfonylureas <sup>12</sup>	Fatigue, dizziness, agitation, confusion, tachycardia, diaphoresis	<b>Dextrose:</b> 0.5–1 g/kg (2–4 mL/kg of D25W) <i>After euglycemia achieved:</i> <b>Octreotide:</b> 1–2 mcg/kg SQ Q6–12 hr if rebound hypoglycemia after dextrose
TCA <sup>15,16</sup>	Seizures, delirium, ventricular arrhythmias, hypotension	<i>For wide QRS complex:</i> <b>NaHCO<sub>3</sub>:</b> 1–2 mEq/kg IV; goal serum pH 7.45–7.55, <i>For torsades:</i> <b>MgSulfate:</b> 50 mg/kg IV over 5–15 min (max dose 2 g)
Warfarin	Bleeding	<b>Phytonadione/Vitamin K<sub>1</sub>:</b> See formulary for dosing

**V. ACETAMINOPHEN OVERDOSE** 4,17,18,19,20

Metabolites are hepatotoxic. Reactive intermediates can cause liver necrosis.

**A. Four Phases of Intoxication**

1. **Phase 1 (first 24 hr):** nonspecific symptoms such as nausea, malaise, vomiting.
2. **Phase 2 (24 to 72 hr):** above symptoms resolve, RUQ pain and hepatomegaly develop. Increase in liver function tests, bilirubin levels, and prothrombin time.
3. **Phase 3 (72 to 96 hr):** return of nonspecific symptoms as well as evidence of liver failure (e.g., jaundice, hypoglycemia, coagulopathy).
4. **Phase 4 (4 days to 2 weeks):** recovery or death.

**B. Treatment Criteria:**

1. **Serum acetaminophen** concentration above the possible toxicity line on the Rumack-Matthew nomogram (Fig. 2-1).
2. **History of ingesting more than 200 mg/kg or 10 g** (whichever is less) and serum concentration not available or time of ingestion not known.

**C. Antidotes: N-Acetylcysteine**

1. **PO:** 140 mg/kg loading dose followed by 70 mg/kg Q4 hr for a total of 72 hours.
2. **IV:** 150 mg/kg N-acetylcysteine IV over 60 minutes followed by 12.5 mg/kg/hr x 4 hours followed by 6.25 mg/kg/hr x 16 hours for a total of 21 hours of infusion. Some patients may require more than 21 hours of N-acetylcysteine.
3. **Liver failure:** treat patients in liver failure with N-acetylcysteine IV, same dose as above. Continue 6.25 mg/kg/hr infusion until resolution of encephalopathy, decreasing aminotransferases and improvement in coagulopathy

**VI. LEAD POISONINGS** 1-23

**A. Etiologies:** paint, dust, soil, drinking water, cosmetics, cookware, toys, and caregivers with occupations and/or hobbies utilizing lead-containing materials or substances.\*

**B. Definition:** Centers for Disease Control and Prevention (CDC) defines an elevated blood lead level (BLL) as  $\geq 5$  mcg/dL.<sup>21</sup>

**C. Overview of Symptoms by BLL:**

1. **BLL >40 mcg/dL:** irritability, vomiting, abdominal pain, constipation, and anorexia.
2. **BLL >70 mcg/dL:** lethargy, seizure, and coma.

**NOTE:** Children may be asymptomatic with lead levels >100 mcg/dL.

**C. Management (Tables 2-4, 2-5, and 2-6):**

\*Children aged 1 to 5 years are at greatest risk of lead poisoning.

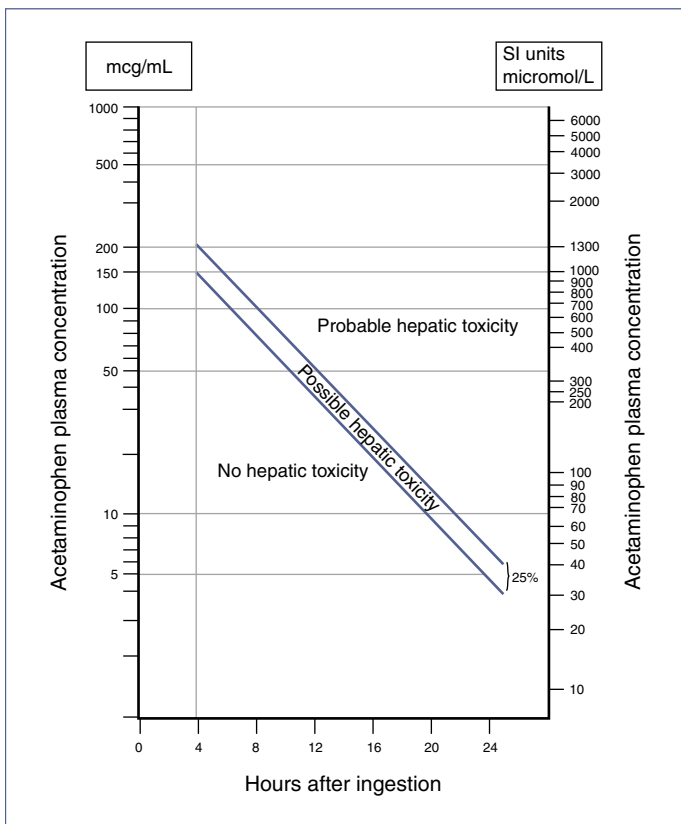


FIGURE 2-1

Semilogarithmic plot of plasma acetaminophen levels versus time. This nomogram is valid for use after acute ingestions of acetaminophen. The need for treatment cannot be extrapolated based on a level before 4 hours. (Based on *Pediatrics* 55:871, 1975 and *Micromedex*.)

### CHELATION THERAPY

1. **Routine indication:** BLL  $\geq$  46 mcg/dL
2. **Overview of antidotes:**
  - A. **Succimer:** 10 mg/kg or 350 mg/m<sup>2</sup> PO Q8 hr x 5 days --> Q12 hr x 14 days
  - B. **Edetate (EDTA) calcium disodium:** 1000 mg/m<sup>2</sup>/24 hr IV infusion as an 8-24 hr infusion OR intermittent dosing divided Q12 hr x 5 days. May repeat course as needed after 2-4 days of no EDTA.

\*Warning: Do not mistake edetate disodium for edetate calcium disodium. Edetate calcium disodium is used for the treatment of lead poisoning.

TABLE 2-4

MANAGEMENT OF LEAD POISONING<sup>21</sup>

Blood Lead Levels (BLL)	Recommended Guidelines
≥ 5 and <10 mcg/dL	<ol style="list-style-type: none"> <li>1. Provide education about reducing environmental lead exposure and reducing dietary lead absorption.*</li> <li>2. Perform environmental assessment in homes built before 1978.</li> <li>3. Follow repeat blood lead testing guidelines (see Table 2-5).</li> </ol>
≥ 10 and ≤45 mcg/dL	<ol style="list-style-type: none"> <li>1. As above for BLL ≥ 5 and &lt;10</li> <li>2. Environmental investigation and lead hazard reduction</li> <li>3. Complete history and exam</li> <li>4. Iron level, complete blood cell count (CBC), abdominal radiography (if ingestion is suspected) with bowel decontamination if indicated</li> <li>5. Neurodevelopmental monitoring</li> </ol>
BLL ≥45 and ≤69 mcg/dL	<ol style="list-style-type: none"> <li>1. As above for BLL ≤45 mcg/dL</li> <li>2. Check free erythrocyte protoporphyrin.</li> <li>3. Administer chelation therapy (See below).</li> </ol>
BLL ≥70 mcg/dL	<ol style="list-style-type: none"> <li>1. As above for BLL ≥45 mcg/dL</li> <li>2. Hospitalize and commence chelation therapy.</li> </ol>

\*Iron, calcium, and vitamin C help minimize absorption of lead.

TABLE 2-5

REPEAT BLOOD LEAD TESTING GUIDELINES<sup>21</sup>

If Screening BLL is:	Time Frame of Confirmation of Screening BLL	Follow-Up Testing (After Confirmatory Testing)	Later Follow-Up Testing After BLL Declining
≥ 5–9 mcg/dL	1–3 months	3 months	6–9 months
10–19 mcg/dL	1 week–1 month*	1–3 months	3–6 months
20–24 mcg/dL	1 week–1 month*	1–3 months	1–3 months
25–44 mcg/dL	1 week–1 month*	2 weeks–1 month	1 month
45–59 mcg/dL	48 weeks	As soon as possible	
60–69 mcg/dL	24 hours		
>70 mcg/dL	Urgently		

\*The higher the blood lead level (BLL) on the screening test, the more urgent the need for confirmatory testing.

- C. **D-penicillamine:** 25–35 mg/kg/day PO in divided doses. Start at 25% of this dose and increase to full dose over 2–3 weeks. Do not give D-penicillamine to patients with a penicillin allergy.
3. **Non-routine indications:** patient with encephalopathy
- A. **Give Dimercaprol (BAL):** 75 mg/m<sup>2</sup> IM Q4 hr x 5 days; immediately after second dose of BAL give EDTA 1500 mg/m<sup>2</sup>/day IV as a continuous infusion or 2–4 divided doses x 5 days

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# Chapter 3

## Procedures

Bradley D. McCammack, MD

3

### I. GENERAL GUIDELINES

#### A. Consent

Before performing any procedure, it is crucial to obtain informed consent from the parent or guardian by explaining the procedure, the indications, any risks involved, and any alternatives. Obtaining consent for life-saving emergency procedures is unnecessary.

#### B. Risks

1. **All invasive procedures involve pain and risk for infection and bleeding.** Specific complications are listed by procedure.
2. **Sedation and analgesia should be planned in advance, and the risks of such explained to the parent and/or patient as appropriate.** In general, 1% lidocaine buffered with sodium bicarbonate is adequate for local analgesia. See Chapter 6 for Analgesia and Procedural Sedation guidelines. Also see the “AAP Guidelines for Monitoring and Management of Pediatric Patients During and After Sedation for Diagnostic and Therapeutic Procedures.”<sup>1</sup>
3. **Universal precautions should be followed for all patient contact that exposes the health care provider to blood, amniotic fluid, pericardial fluid, pleural fluid, synovial fluid, cerebrospinal fluid (CSF), semen, or vaginal secretions.**
4. **Proper sterile technique is essential to achieving good wound closure, decreasing transmittable diseases, and preventing wound contamination.**
5. **Videos are available for some procedures via *New England Journal of Medicine’s* “Videos in Clinical Medicine.”** Links to videos will be listed in the respective sections when available.

### II. BLOOD SAMPLING

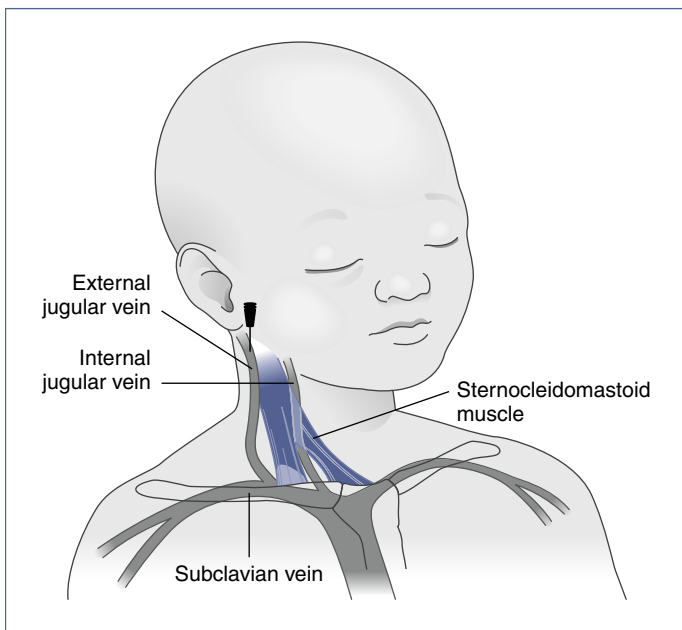
#### A. Heelstick and Fingerstick<sup>2</sup>

1. **Indications:** Blood sampling in infants for laboratory studies unaffected by hemolysis
2. **Complications:** Infection, bleeding, osteomyelitis
3. **Procedure:**
  - a. Warm heel or finger.
  - b. Clean with alcohol.
    - (1) Puncture heel using a lancet on the lateral part of the heel, avoiding the posterior area.
    - (2) Puncture finger using a lancet on the palmar lateral surface of the finger near the tip.

- c. Wipe away the first drop of blood, then collect the sample using a capillary tube or container.
- d. Alternate between squeezing blood from the leg toward the heel (or from the hand toward the finger) and then releasing the pressure for several seconds.

### B. External Jugular Puncture<sup>3</sup>

- 1. **Indications:** Blood sampling in patients with inadequate peripheral vascular access or during resuscitation
- 2. **Complications:** Infection, bleeding, pneumothorax
- 3. **Procedure** (Fig. 3-1):
  - a. Restrain infant securely. Place infant with head turned away from side of blood sampling. Position with towel roll under shoulders or with head over side of bed to extend neck and accentuate the posterior margin of the sternocleidomastoid muscle on the side of the venipuncture.
  - b. Prepare area in a sterile fashion.
  - c. The external jugular vein will distend if its most proximal segment is occluded or if the child cries. The vein runs from the angle of the mandible to the posterior border of the lower third of the sternocleidomastoid muscle.



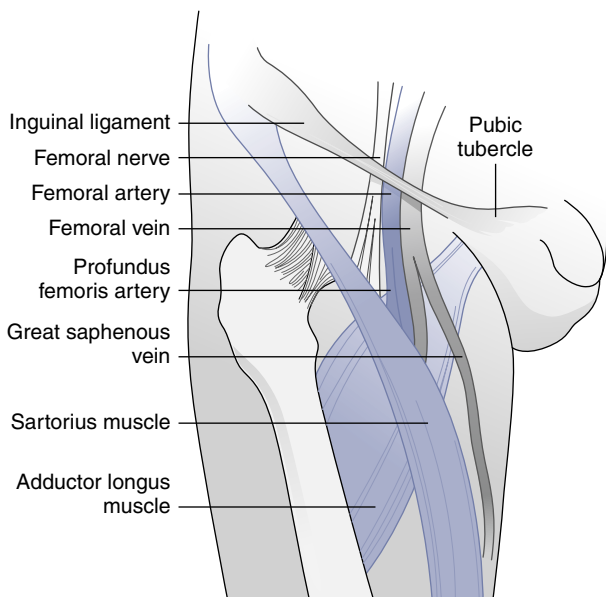
**FIGURE 3-1**

External jugular cannulation. (From Dieckmann R, Fiser D, Selbst S. Pediatric Emergency and Critical Care Procedures. St. Louis: Mosby, 1997.)

- d. With continuous negative suction on the syringe, insert the needle at about a 30-degree angle to the skin. Continue as with any peripheral venipuncture.
- e. Apply a sterile dressing, and put pressure on the puncture site for 5 minutes.

### C. Femoral Artery and Femoral Vein Puncture<sup>3,4</sup>

1. **Indications:** Venous or arterial blood sampling in patients with inadequate vascular access or during resuscitation.
2. **Contraindications:** Femoral puncture is particularly hazardous in neonates and *not* recommended in this age group. There is also a risk in children for trauma to the femoral head and joint capsule. Avoid femoral punctures in children who have thrombocytopenia or coagulation disorders and in those who are scheduled for cardiac catheterization.
3. **Complications:** Infection, bleeding, hematoma of femoral triangle, thrombosis of vessel, osteomyelitis, septic arthritis of hip.
4. **Procedure** (Fig. 3-2):
  - a. Hold child securely in frog-leg position with the hips flexed and abducted. It may help to place a roll under the hips.



**FIGURE 3-2**

Femoral artery and vein anatomy. (From Dieckmann R, Fiser D, Selbst S. Pediatric Emergency and Critical Care Procedures. St. Louis: Mosby, 1997.)

- b. Prepare area in sterile fashion.
- c. Locate femoral pulse just distal to the inguinal crease (note that vein is medial to pulse). Insert needle 2 cm distal to the inguinal ligament and 0.5 to 0.75 cm into the groin. Aspirate while maneuvering the needle until blood is obtained.

**NOTE:** The right femoral vein is easier to cannulate than left owing to straighter path to inferior vena cava.

- d. Apply direct pressure for minimum of 5 minutes.

#### **D. Radial Artery Puncture and Catheterization<sup>3,4</sup>**

- 1. **Indications:** Arterial blood sampling or frequent blood gases and continuous blood pressure monitoring in an intensive care setting.
- 2. **Complications:** Infection, bleeding, occlusion of artery by hematoma or thrombosis, ischemia if ulnar circulation is inadequate.
- 3. **Procedure:**
  - a. Before procedure, test adequacy of ulnar blood flow with the Allen test. Clench the hand while simultaneously compressing ulnar and radial arteries. The hand will blanch. Release pressure from the ulnar artery, and observe the flushing response. Procedure is safe to perform if entire hand flushes.
  - b. Locate the radial pulse. It is optional to infiltrate the area over the point of maximal impulse with lidocaine. Avoid infusion into the vessel by aspirating before infusing. Prepare the site in sterile fashion.
    - (1) Puncture: Insert butterfly needle attached to a syringe at a 30- to 60-degree angle over the point of maximal impulse. Blood should flow freely into the syringe in a pulsatile fashion. Suction may be required for plastic tubes. Once the sample is obtained, apply firm, constant pressure for 5 minutes and then place a pressure dressing on the puncture site.
    - (2) Catheter placement: Secure the patient's hand to an arm board. Leave the fingers exposed to observe any color changes. Prepare the wrist with sterile technique and infiltrate over the point of maximal impulse with 1% lidocaine. Make a small skin puncture over the point of maximal impulse with a needle, then discard the needle. Insert an intravenous (IV) catheter with its needle through the puncture site at a 30-degree angle to the horizontal. Pass the needle and catheter through the artery to transfix it, then withdraw the needle. Very slowly, withdraw the catheter until free flow of blood is noted, then advance the catheter and secure in place using sutures or tape. Seldinger technique using a guidewire can also be used. Apply a sterile dressing. Infuse heparinized isotonic fluid (per protocol) at 1 mL/hr. A pressure transducer may be attached to monitor blood pressure.

**NOTE:** Do not infuse any medications, blood products, or hypotonic or hypertonic solutions through an arterial line.
    - (3) Suggested size of arterial catheters based on weight:
      - (a) Infant (<10 kg): 24G or 2.5Fr, 2.5 cm

(b) Child (10 to 40 kg): 22G or 2.4Fr, 2.5 cm

(c) Adolescent (>40 kg): 20G

4. **A video on radial artery catheterization is available on the New England Journal of Medicine's website.**

#### E. Posterior Tibial and Dorsalis Pedis Artery Puncture<sup>4</sup>

1. **Indications:** Arterial blood sampling when radial artery puncture is unsuccessful or inaccessible.
2. **Complications:** Infection, bleeding, ischemia if circulation is inadequate
3. **Procedure (see Section II.D for technique):**
  - a. Posterior tibial artery: Puncture the artery posterior to medial malleolus while holding foot in dorsiflexion.
  - b. Dorsalis pedis artery: Puncture the artery at dorsal midfoot between first and second toes while holding foot in plantar flexion.

3

### III. VASCULAR ACCESS

#### A. Peripheral Intravenous Placement

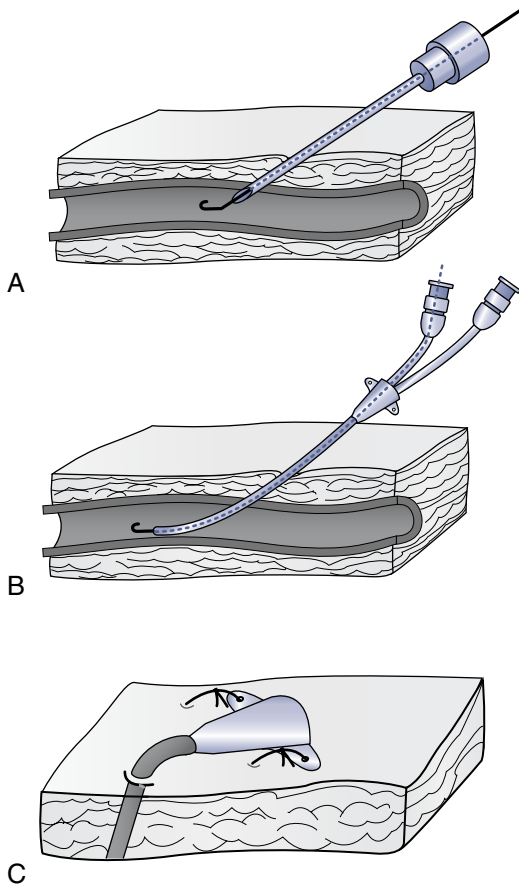
1. **Indications:** To obtain access to peripheral venous circulation to deliver fluid, medications, or blood products.
2. **Complications:** Thrombosis, infection.
3. **Procedure:**
  - a. Choose IV placement site and prepare with alcohol.
  - b. Apply tourniquet and then insert IV catheter, bevel up, at angle almost parallel to the skin, advancing until a *flash* of blood is seen in the catheter hub. Advance the plastic catheter only, remove the needle, and secure the catheter.
  - c. After removing tourniquet, attach T connector filled with saline to the catheter, flush with normal saline (NS) to ensure patency of the IV line.
4. **A video on peripheral IV placement is available on the New England Journal of Medicine's website.**

#### B. Central Venous Catheter Placement<sup>3,5-7</sup>

1. **Indications:** To obtain emergency access to central venous circulation, monitor central venous pressure, deliver high-concentration parenteral nutrition or prolonged IV therapy, or infuse blood products or large volumes of fluid.
2. **Complications:** Infection, bleeding, arterial or venous perforation, pneumothorax, hemothorax, thrombosis, catheter fragment in circulation, air embolism.
3. **Ultrasound guidance:** Quickly becoming standard among health care facilities to aid placement of central venous catheters. It has been shown to reduce failure and complication rates when effectively implemented.
4. **Access sites:**
  - a. External jugular vein
  - b. Subclavian vein: Least common site in children owing to increased complications
  - c. Internal jugular vein: Contraindicated with elevated intracranial pressure
  - d. Femoral vein: Contraindicated with severe abdominal trauma

5. **Procedure:** Seldinger technique (Fig. 3-3)

- a. Secure patient, prepare site, and drape according to the following guidelines for sterile technique<sup>7</sup>:
- (1) Wash hands.
  - (2) Wear hat, mask, eye shield, sterile gloves, and sterile gown.

**FIGURE 3-3**

Seldinger technique. **A**, Guidewire is placed through introducer needle into lumen of vein. **B**, Catheter is advanced into vein lumen along guidewire. **C**, Hub of catheter is secured to skin with suture. (Modified from Fuhrman B, Zimmerman J. *Pediatric Critical Care*. 4th ed. Philadelphia: Mosby, 2011.)

- (3) Prep procedure site for 30 seconds (chlorhexidine), and allow to dry for an additional 30 seconds (in groin, scrub for 2 minutes, and allow to dry for 1 minute).
- (4) Use sterile technique to drape the site.
- b. Insert needle, applying negative pressure to locate vessel.
- c. When there is blood return, insert a guidewire through the needle into the vein. Watch cardiac monitor for ectopy.
- d. Remove the needle, firmly holding the guidewire.
- e. Slip a catheter that has been preflushed with sterile saline over the wire into the vein in a twisting motion. The entry site may be enlarged with a small skin incision or dilator. Pass the entire catheter over the wire until the hub is at the skin surface. Slowly remove the wire, secure the catheter by suture, and attach IV infusion.
- f. Apply a sterile dressing over the site.
- g. For neck vessels, obtain a chest radiograph to rule out pneumothorax.
- h. A video on [central venous catheterization](#) is available on the New England Journal of Medicine's website.
6. **Approach:**
  - a. External jugular (see [Fig. 3-1](#)): Place patient in 15- to 20-degree Trendelenburg position. Turn the head 45 degrees to the contralateral side. Enter the vein at the point where it crosses the sternocleidomastoid muscle.
  - b. Internal jugular ([Fig. 3-4](#)): Place patient in 15- to 20-degree Trendelenburg position. Hyperextend the neck to tense the sternocleidomastoid muscle, and turn head away from the site of line placement. Palpate the sternal and clavicular heads of the muscle, and enter at the apex of the triangle formed. An alternative landmark for puncture is halfway between the sternal notch and tip of the mastoid process. Insert the needle at a 30-degree angle to the skin, and aim toward the ipsilateral nipple. When blood flow is obtained, continue with Seldinger technique. Right side is preferable because of straight course to right atrium, absence of thoracic duct, and lower pleural dome on right side. The internal jugular vein runs lateral to the carotid artery.
  - c. Subclavian vein ([Fig. 3-5](#)): Position child in Trendelenburg position with a towel roll under thoracic spine to hyperextend the back. Aim the needle under the distal third of the clavicle toward the sternal notch. When blood flow is obtained, continue with Seldinger technique.
    - (1) A video on [subclavian venous catheter placement](#) is available on the New England Journal of Medicine's website.
  - d. Femoral vein ([Fig. 3-6](#)): Hold child securely with the hip flexed and abducted. Locate the femoral pulse just distal to the inguinal crease. In infants, vein is 5 to 6 mm *medial* to arterial pulse. In adolescents, vein is usually 10 to 15 mm *medial* to the pulse. Place the thumb of the nondominant hand on the femoral artery. Insert the needle medial to the thumb. The needle should enter the skin 2 to 3 cm distal to the inguinal ligament at a 30-degree angle to avoid entering the abdomen. When blood flow is obtained, continue with Seldinger technique.



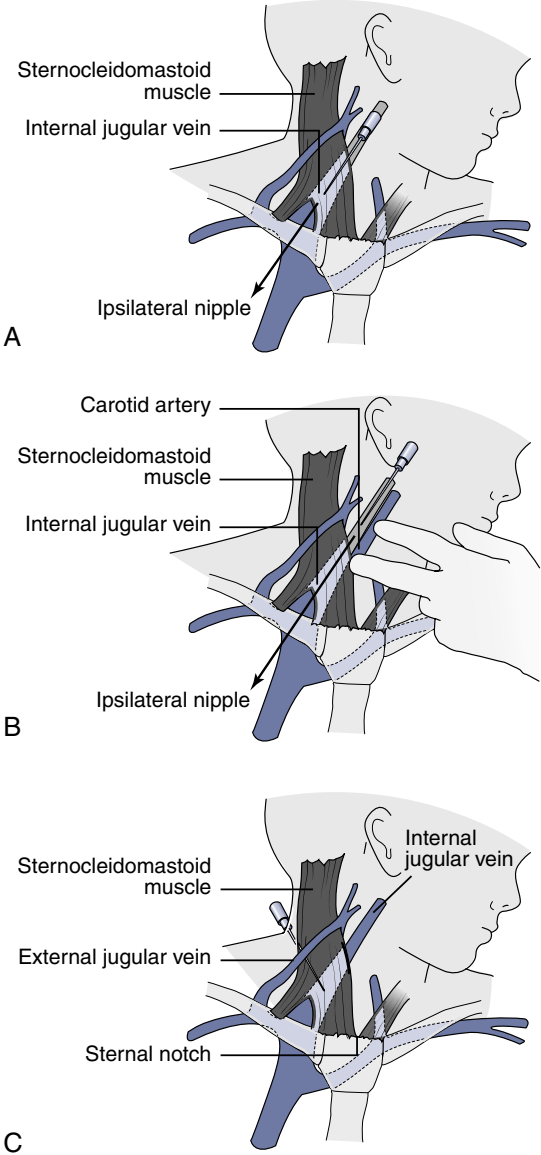
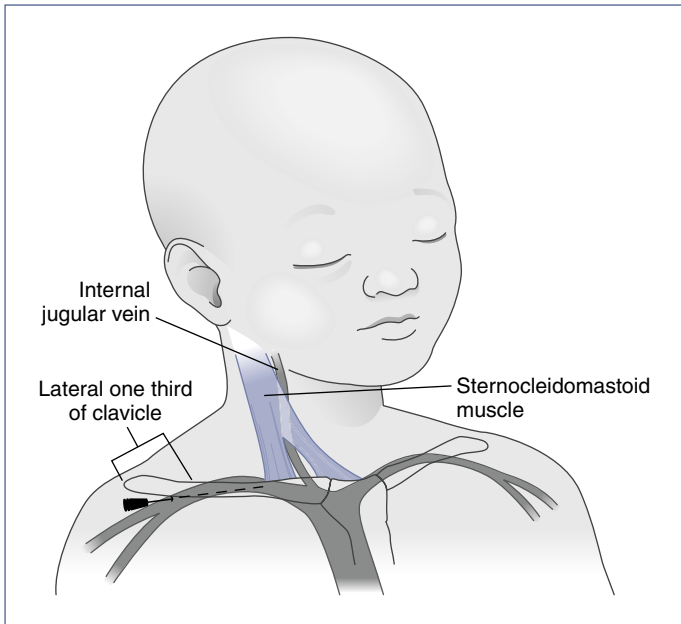


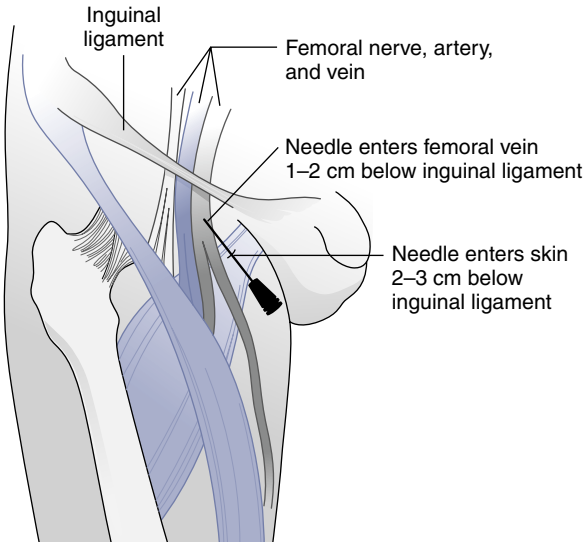
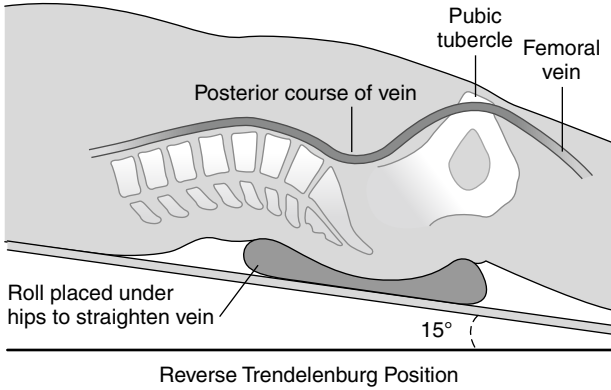
FIGURE 3-4

Approaches to the internal jugular vein. Patient is supine in slight Trendelenburg position, with neck extended over a shoulder roll and head rotated away from side of approach. **A**, Middle approach. Introducer needle enters at apex of a triangle formed by the heads of the sternocleidomastoid muscle and clavicle and is directed toward the ipsilateral nipple at an angle of approximately 30 degrees with the skin. **B**, Anterior approach. Carotid pulse is palpated and may be slightly retracted medially. Introducer needle enters along anterior margin of sternocleidomastoid about halfway between sternal notch and mastoid process and is directed toward the ipsilateral nipple. **C**, Posterior approach. Introducer needle enters at the point where external jugular vein crosses posterior margin of sternocleidomastoid and is directed under its head toward sternal notch. (Modified from Fuhrman B, Zimmerman J. Pediatric Critical Care. 4th ed. Philadelphia: Mosby, 2011.)



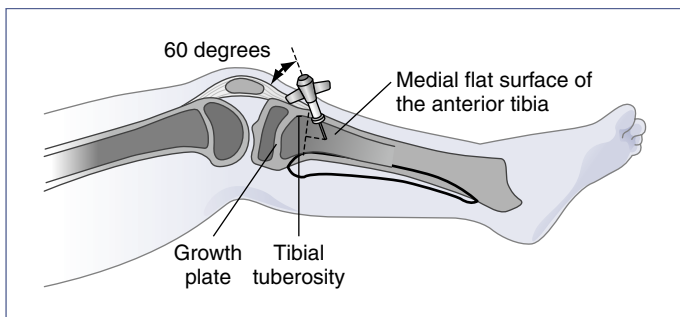
**FIGURE 3-5**

Subclavian vein cannulation. (From Dieckmann R, Fiser D, Selbst S. Pediatric Emergency and Critical Care Procedures. St. Louis: Mosby, 1997.)



**FIGURE 3-6**

Femoral vein cannulation. (From Dieckmann R, Fiser D, Selbst S. Pediatric Emergency and Critical Care Procedures. St. Louis: Mosby, 1997.)

**FIGURE 3-7**

Intraosseous needle placement using standard anterior tibial approach. Insertion point is in the midline on medial flat surface of anterior tibia, 1 to 3 cm (2 fingerbreadths) below tibial tuberosity. (From Dieckmann R, Fiser D, Selbst S. Pediatric Emergency and Critical Care Procedures. St. Louis: Mosby, 1997.)

- (1) A video on [femoral venous catheterization](#) is available on the New England Journal of Medicine's website.

### C. Intraosseous (IO) Infusion<sup>3,4</sup> (Fig. 3-7)

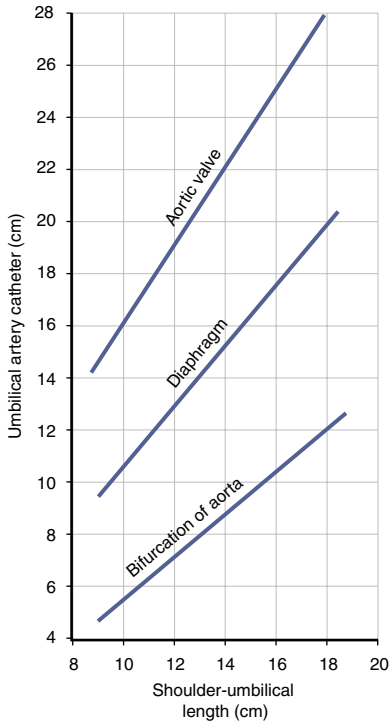
1. **Indications:** Obtain emergency access in children during life-threatening situations. This is very useful during cardiopulmonary arrest, shock, burns, and life-threatening status epilepticus. IO line can be used to infuse medications, blood products, or fluids. The IO needle should be removed once adequate vascular access has been established.
2. **Complications:**
  - a. Complications are rare, particularly with correct technique. Frequency of complications increases with prolonged infusions.
  - b. Extravasation of fluid from incomplete cortex penetration, infection, bleeding, osteomyelitis, compartment syndrome, fat embolism, fracture, epiphyseal injury.
3. **Sites of entry (in order of preference):**
  - a. Anteromedial surface of the proximal tibia, 2 cm below and 1 to 2 cm medial to the tibial tuberosity on the flat part of the bone (see Fig. 3-7)
  - b. Distal femur 3 cm above the lateral condyle in the midline
  - c. Medial surface of the distal tibia 1 to 2 cm above the medial malleolus (may be a more effective site in older children)
  - d. Anterosuperior iliac spine at an angle of 90 degrees to the long axis of the body
4. **Procedure:**
  - a. Prepare the selected site in sterile fashion if situation allows.
  - b. If the child is conscious, anesthetize the puncture site down to the periosteum with 1% lidocaine (optional in emergency situations).
  - c. Choose between manual IO or drill-powered IO insertion device:
    - (1) For manual IO needle: Insert a 15- to 18-gauge IO needle perpendicular to skin at angle away from epiphyseal plate, and advance

to the periosteum. With a boring rotary motion, penetrate through the cortex until there is a decrease in resistance, indicating that you have reached the marrow. The needle should stand firmly without support. Secure the needle carefully.

- (2) For drill-powered IO needle: Enter skin with the needle perpendicular to the skin, as with the manual needle, and gently power the drill or simply press the needle until you meet the periosteum. Apply easy pressure while gently depressing the drill trigger until you feel a “pop” or a sudden decrease in resistance. Remove the drill while holding the needle steady to ensure stability prior to securing the needle. Use an EZ-IO AD for patients >40 kg, and use EZ-IO PD for patients >6 kg and <40 kg.
- d. Remove the stylet and attempt to aspirate marrow. (Note that it is not necessary to aspirate marrow.) Flush with 10 to 20 mL of crystalloid solution. Observe for fluid extravasation. Marrow can be sent for determination of glucose levels, chemistries, blood type and cross-match, hemoglobin, blood gas analysis, and cultures.
- e. Attach standard IV tubing. Any crystalloid, blood product, or drug that may be infused into a peripheral vein may also be infused into the IO space, but increased pressure (through pressure bag or push) is necessary for infusion. There is a high risk for obstruction if continuous high-pressure fluids are not flushed through the IO needle.
5. **A video on IO catheter placement is available on the New England Journal of Medicine's website.**

#### **D. Umbilical Artery (UA) and Umbilical Vein (UV) Catheterization<sup>3</sup>**

1. **Indications:** Vascular access (via UV), blood pressure (via UA), and blood gas (via UA) monitoring in critically ill neonates.
2. **Complications:** Infection, bleeding, hemorrhage, perforation of vessel; thrombosis with distal embolization; ischemia or infarction of lower extremities, bowel, or kidney; arrhythmia if catheter is in the heart; air embolus.
3. **Caution:** UA catheterization should never be performed if omphalitis or peritonitis is present. It is contraindicated in the presence of possible necrotizing enterocolitis or intestinal hypoperfusion.
4. **Line placement:**
  - a. Arterial line: Low line vs. high line.
    - (1) Low line: Tip of catheter should lie just above the aortic bifurcation between L3 and L5. This avoids renal and mesenteric arteries near L1, possibly decreasing the incidence of thrombosis or ischemia.
    - (2) High line: Tip of catheter should be above the diaphragm between T6 and T9. A high line may be recommended in infants weighing less than 750 g, in whom a low line could easily slip out.
  - b. UV catheters should be placed in the inferior vena cava above the level of the ductus venosus and the hepatic veins and below the level of the right atrium.

**FIGURE 3-8**

Umbilical artery catheter length.

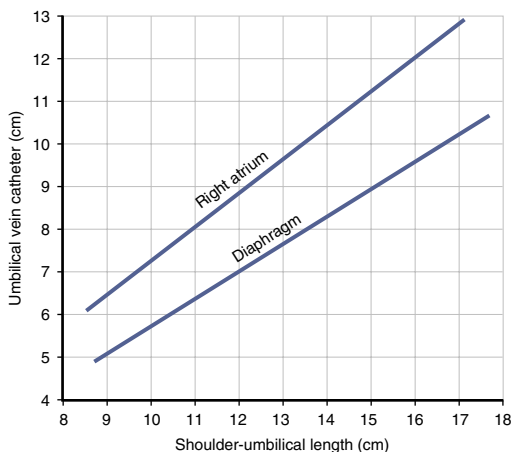
c. Catheter length: Determine the length of catheter required using either a standardized graph or the regression formula. Add length for the height of the umbilical stump.

- (1) Standardized graph: Determine the shoulder-umbilical length by measuring the perpendicular line dropped from the tip of the shoulder to the level of the umbilicus. Use the graph in Fig. 3-8 to determine the arterial catheter length, and the graph in Fig. 3-9 to determine venous catheter length.
- (2) Birth weight (BW) regression formula:

$$\text{Low line : UA catheter length (cm)} = \text{BW (kg)} + 7.$$

$$\text{High line : UA catheter length (cm)} = [3 \times \text{BW (kg)}] + 9$$

$$\text{UV catheter length (cm)} = [0.5 \times \text{high line UA (cm)}] + 1$$

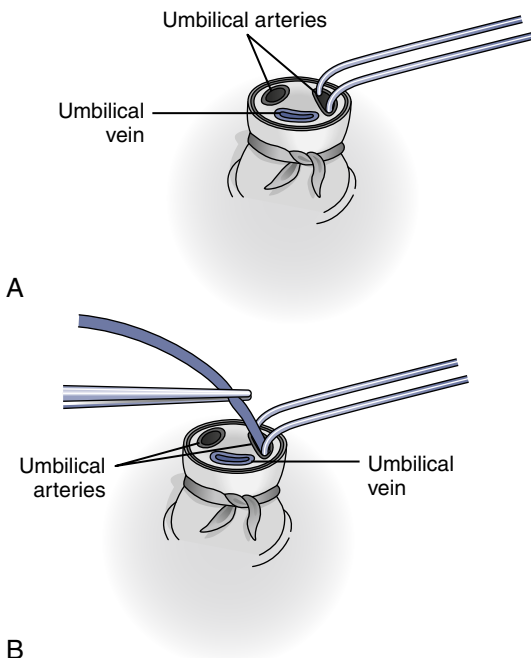
**FIGURE 3-9**

Umbilical vein catheter length.

**NOTE:** Formula may not be appropriate for infants who are small for gestational age (SGA) or large for gestational age (LGA).

**5. Procedure for UA line (Fig. 3-10):**

- Determine the length of the catheter to be inserted for either high (T6–T9) or low (L3–L5) position.
- Restrain infant. Maintain the infant's temperature during the procedure. Prepare and drape the umbilical cord and adjacent skin using sterile technique.
- Flush the catheter with sterile saline solution before insertion. Ensure there are no air bubbles in the catheter or attached syringe.
- Place sterile umbilical tape around the base of the cord. Cut through the cord horizontally about 1.5 to 2 cm from the skin; tighten the umbilical tape to prevent bleeding.
- Identify the one large, thin-walled umbilical vein and two smaller, thick-walled arteries. Use one tip of open, curved forceps to gently probe and dilate one artery. Use both points of closed forceps, and dilate artery by allowing forceps to open gently.
- Grasp the catheter 1 cm from its tip with toothless forceps, and insert the catheter into the lumen of the artery. Aim the tip toward the feet, and gently advance the catheter to the desired distance. *Do not force.* If resistance is encountered, try loosening umbilical tape, applying steady and gentle pressure, or manipulating the angle of the umbilical cord to skin. Often the catheter cannot be advanced because of creation of a “false luminal tract.” There should be good blood return when the catheter enters the iliac artery.

**FIGURE 3-10**

Placement of umbilical arterial catheter. **A**, Dilating lumen of umbilical artery. **B**, Insertion of umbilical artery catheter. **C**, Securing catheter to abdominal wall using bridge method of taping. (From Dieckmann R, Fiser D, Selbst S. Pediatric Emergency and Critical Care Procedures. St. Louis: Mosby, 1997.)

- g. Radiographically confirm catheter tip position. Secure catheter with a suture through the cord, a marker tape, and a tape bridge. The catheter may be pulled back but *not* advanced once the sterile field is broken.
- h. Observe for complications: Blanching or cyanosis of lower extremities, perforation, thrombosis, embolism, or infection. If any complications occur, the catheter should be removed.
- i. Use isotonic fluids, which contain 0.5 units/mL of heparin. Never use hypo-osmolar fluids in the UA.

**NOTE:** There are no definitive guidelines on feeding with a UA catheter in place. There is concern (up to 24 hours after removal) that the UA catheter or thrombus may interfere with intestinal perfusion. A risk-to-benefit assessment should be individualized.

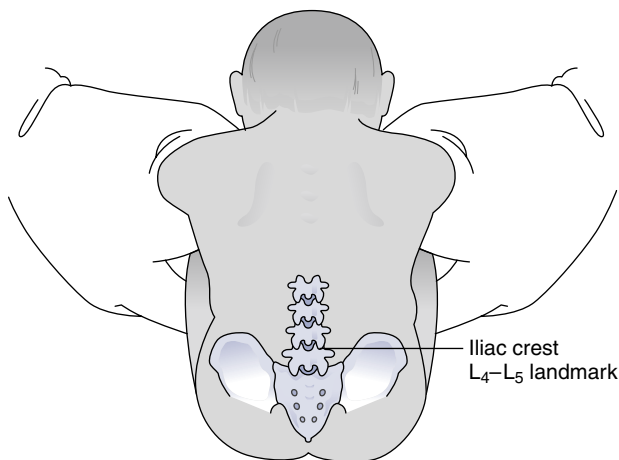


**6. Procedure for UV line (Fig. 3-10):**

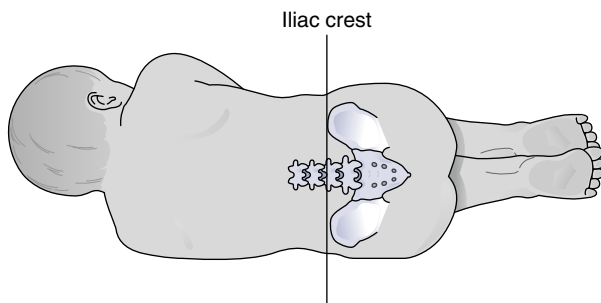
- a. Follow steps “a” through “d” for UA catheter placement, but determine catheter length using Fig. 3-9.
- b. Isolate the thin-walled umbilical vein, clear thrombi with forceps, and insert catheter, aiming the tip toward the right shoulder. Gently advance the catheter to the desired distance. *Do not force.* If resistance is encountered, try loosening the umbilical tape, applying steady and gentle pressure, or manipulating the angle of the umbilical cord to skin. Resistance is commonly met at the abdominal wall and again at the portal system. *Do not* infuse anything into liver.
- c. Radiographically confirm catheter tip position. Secure catheter as described in step “g” for UA placement.
7. **A video on UV/UA line placement is available on the New England Journal of Medicine’s website.**

**IV. BODY FLUID SAMPLING****A. Lumbar Puncture<sup>3,4</sup>**

1. **Indications:** Examination of spinal fluid for suspected infection or malignancy, instillation of intrathecal chemotherapy, or measurement of opening pressure.
2. **Complications:** Local pain, infection, bleeding, spinal fluid leak, hematoma, spinal headache, acquired epidermal spinal cord tumor (caused by implantation of epidermal material into spinal canal if no stylet is used on skin entry).
3. **Cautions and contraindications:**
  - a. Increased intracranial pressure (ICP): Before lumbar puncture (LP), perform fundoscopic examination. Presence of papilledema, retinal hemorrhage, or clinical suspicion of increased ICP may be contraindications to the procedure. A sudden drop in intraspinal pressure by rapid release of CSF may cause fatal herniation. If LP is to be performed, proceed with extreme caution. Computed tomography (CT) may be indicated before LP if there is suspected intracranial bleeding, focal mass lesion, or increased ICP. A normal CT scan does not rule out increased ICP but usually excludes conditions that may put the patient at risk for herniation. Decision to obtain CT should not delay appropriate antibiotic therapy if indicated.
  - b. Bleeding diathesis: Platelet count  $>50,000/\text{mm}^3$  is desirable before LP, and correction of any clotting factor deficiencies can minimize risk for bleeding and subsequent cord or nerve root compression.
  - c. Overlying skin infection may result in inoculation of CSF with organisms.
  - d. LP should be deferred in an unstable patient, and appropriate therapy should be initiated, including antibiotics if indicated.
4. **Procedure:**
  - a. Apply local anesthetic cream if sufficient time is available.
  - b. Position child in either the sitting position (Fig. 3-11) or lateral recumbent position (Fig. 3-12), with hips, knees, and neck flexed. Keep shoulders and hips aligned (perpendicular to examining table in recumbent

**FIGURE 3-11**

Lumbar puncture site in sitting position. (From Dieckmann R, Fiser D, Selbst S. *Pediatric Emergency and Critical Care Procedures*. St. Louis: Mosby, 1997.)

**FIGURE 3-12**

Lumbar puncture site in lateral (recumbent) position. (From Dieckmann R, Fiser D, Selbst S. *Pediatric Emergency and Critical Care Procedures*. St. Louis: Mosby, 1997.)

position) to avoid rotating the spine. *Do not* compromise a small infant's cardiorespiratory status with positioning.

- c. Locate the desired intervertebral space (either L3-4 or L4-5) by drawing an imaginary line between the top of the iliac crests.
- d. Prepare the skin in sterile fashion. Drape conservatively to make monitoring the infant possible. Use a 20G to 22G spinal needle with stylet

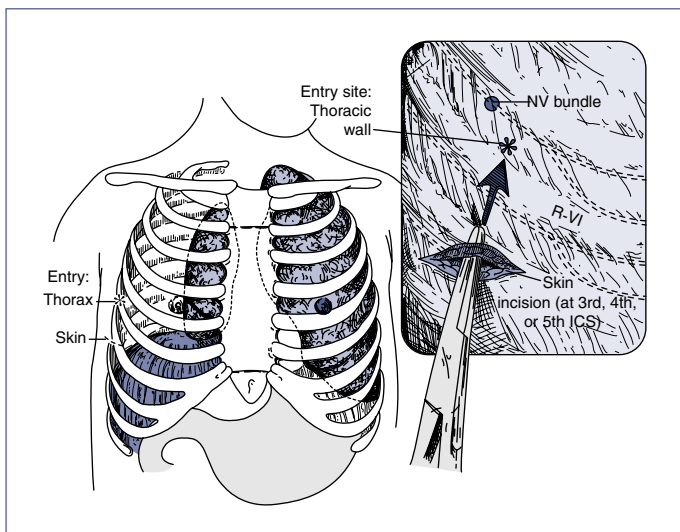
(1.5 inch for children <12 years, 3.5 inches for children ≥12 years).

A smaller-gauge needle will decrease the incidence of spinal headache and CSF leak.

- e. Overlying skin and interspinous tissue can be anesthetized with 1% lidocaine using a 25G needle.
  - f. Puncture the skin in the midline just caudad to the palpated spinous process, angling slightly cephalad toward the umbilicus. Advance several millimeters at a time, and withdraw stylet frequently to check for CSF flow. Needle may be advanced without the stylet once it is completely through the skin. In small infants, one may *not* feel a change in resistance or “pop” as the dura is penetrated.
  - g. If resistance is met initially (you hit bone), withdraw needle to the skin surface and redirect angle slightly.
  - h. Send CSF for appropriate studies (see Chapter 27 for normal values). Send the first tube for culture and Gram stain, second tube for measurement of glucose and protein levels, and last tube for cell count and differential. An additional tube can be collected for viral cultures, polymerase chain reaction (PCR), or CSF metabolic studies if indicated. If subarachnoid hemorrhage or traumatic tap is suspected, send the first and fourth tubes for cell count, and ask the laboratory to examine the CSF for xanthochromia.
  - i. Accurate measurement of CSF pressure can be made only with the patient lying quietly on his or her side in an unflexed position. It is not a reliable measurement in the sitting position. Once free flow of spinal fluid is obtained, attach the manometer and measure CSF pressure. Opening pressure is recorded as the level at which CSF is steady.
5. **A video on lumbar punctures is available on the New England Journal of Medicine's website.**

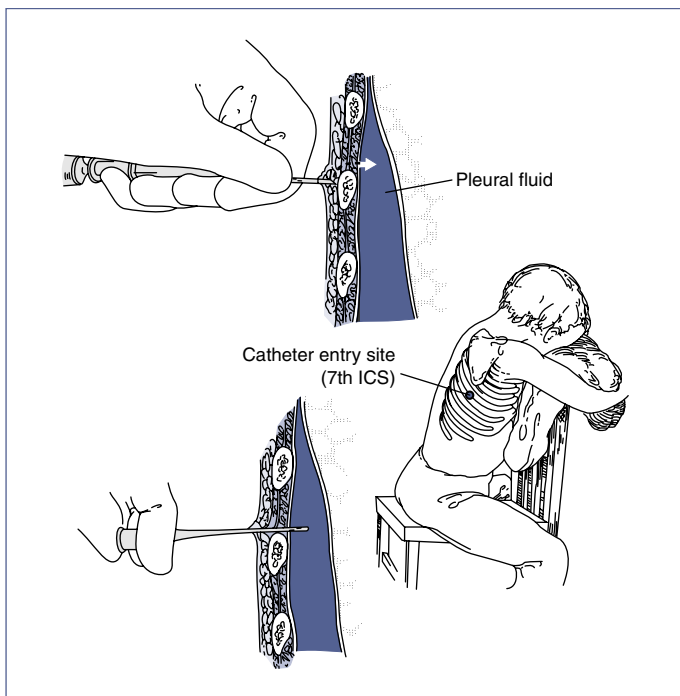
## **B. Chest Tube Placement and Thoracentesis<sup>3,6</sup>**

1. **Indications:** Evacuation of a pneumothorax, hemothorax, chylothorax, large pleural effusion, or empyema for diagnostic or therapeutic purposes.
2. **Complications:** Infection, bleeding, pneumothorax, hemothorax, pulmonary contusion or laceration, puncture of diaphragm, spleen, or liver, or bronchopleural fistula.
3. **Procedure:** Needle decompression.  
**NOTE:** For tension pneumothoraces, it is imperative to attempt decompression quickly by inserting a large-bore needle (14G–22G, based on size) in the anterior second intercostal space in the midclavicular line. Insert needle over superior aspect of rib margin to avoid vascular structures.
- a. When pleural space is entered, attach catheter to a three-way stopcock and syringe, and aspirate air.
- b. Subsequent insertion of a chest tube is still necessary.
4. **Procedure (Fig. 3-13):** Chest tube insertion.  
 (See inside front cover for chest tube sizes.)
  - a. Position child supine or with affected side up and arm restrained over the head.
  - b. Point of entry is the third to fifth intercostal space in the mid- to anterior axillary line, usually at the level of the nipple (avoid breast tissue).

**FIGURE 3-13**

Technique for insertion of chest tube. ICS, Intercostal space; NV, neurovascular; R-VI, sixth rib. (Modified from Fleisher G, Ludwig S. *Pediatric Emergency Medicine*. 3rd ed. Baltimore: Williams & Wilkins, 2000.)

- c. Prepare and drape in sterile fashion.
  - d. Patient may require sedation (see Chapter 6). Locally anesthetize skin, subcutaneous tissue, periosteum of rib, chest wall muscles, and pleura with 1% lidocaine.
  - e. Make sterile 1- to 3-cm incision one intercostal space below desired insertion point, and bluntly dissect with a hemostat through tissue layers until the superior portion of the rib is reached, avoiding the neurovascular bundle on the inferior portion of the rib.
  - f. Push hemostat over the top of the rib, through pleura, and into pleural space. Enter the pleural space cautiously and not deeper than 1 cm. Spread hemostat to open, place chest tube in clamp, and guide through entry site to desired distance.
  - g. For a pneumothorax, insert tube anteriorly toward the apex. For a pleural effusion, direct tube inferiorly and posteriorly.
  - h. Secure chest tube with purse-string sutures in which suture is first tied at the skin, then wrapped around the tube once and tied at the tube.
  - i. Attach to a drainage system with 20 to 30 cm H<sub>2</sub>O pressure.
  - j. Apply a sterile occlusive dressing.
  - k. Confirm position and function with chest radiograph.
5. **A video on chest tube insertion is available on the New England Journal of Medicine's website.**

**FIGURE 3-14**

Thoracentesis. ICS, Intercostal space. (Modified from Fleisher G, Ludwig S. Pediatric Emergency Medicine. 3rd ed. Baltimore: Williams & Wilkins, 2000.)

**6. Procedure:** Thoracentesis (Fig. 3-14)

- Confirm fluid in pleural space by clinical examination and radiographs or ultrasonography.
- If possible, place child in sitting position leaning over table; otherwise place supine.
- Point of entry is usually in the seventh intercostal space and posterior axillary line.
- Prepare and drape area in sterile fashion.
- Anesthetize skin, subcutaneous tissue, rib periosteum, chest wall, and pleura with 1% lidocaine.
- Advance an 18G–22G IV catheter or large-bore needle attached to a syringe onto the rib, and then “walk” over the superior aspect into the pleural space while providing steady negative pressure; often a popping sensation is generated. *Be careful to not advance too far into the pleural cavity.* If an IV or pigtail catheter (with guidewire) is used, the soft catheter may be advanced into the pleural space, aiming downward.

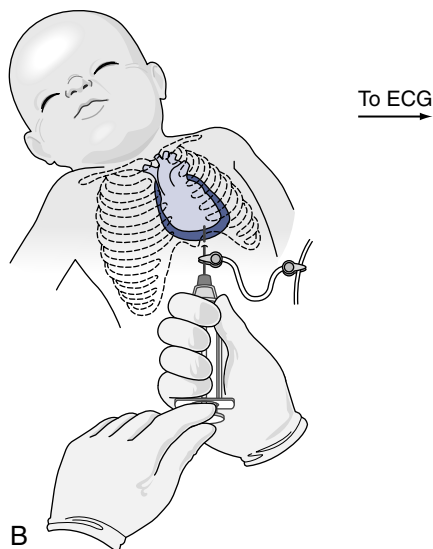
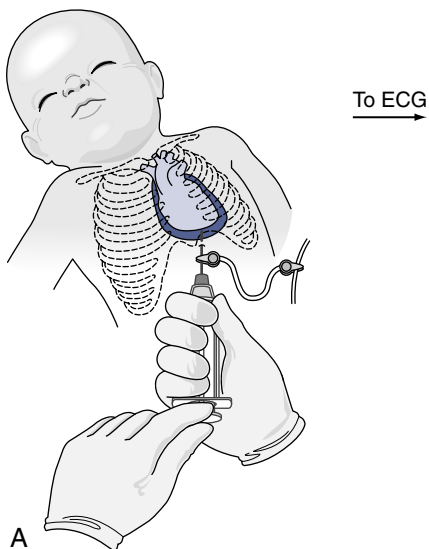
- g. Attach syringe and stopcock device to remove fluid for diagnostic studies and symptomatic relief (see Chapter 27 for evaluation of pleural fluid).
- h. After removing needle or catheter, place an occlusive dressing over the site and obtain a chest radiograph to rule out pneumothorax.
7. **A video on thoracentesis is available on the New England Journal of Medicine's website.**

### C. Pericardiocentesis<sup>3,6</sup>

1. **Indications:** To obtain pericardial fluid in cardiac tamponade emergently or nonemergently for diagnostic or therapeutic purposes.
2. **Complications:** Bleeding, infection, puncture of cardiac chamber, cardiac dysrhythmia, hemopericardium or pneumopericardium, pneumothorax, hemothorax, cardiac arrest, death.
3. **Procedure (Figs. 3-15 and 3-16):**
  - a. Unless contraindicated, provide sedation and/or analgesia for the patient. Monitor electrocardiogram (ECG).
  - b. Place patient at a 30-degree angle (reverse Trendelenburg). Have patient secured.
  - c. Prepare and drape puncture site in sterile fashion. A drape across upper chest is unnecessary and may obscure important landmarks.
  - d. Anesthetize puncture site with 1% lidocaine.
  - e. Insert an 18G or 20G needle just to the left of the xiphoid process, 1 cm inferior to the bottom rib at about a 45-degree angle to the skin.
  - f. While gently aspirating, advance needle toward the patient's left shoulder until pericardial fluid is obtained.
  - g. Upon entering the pericardial space, clamp the needle with a hemostat at the skin edge to prevent further penetration. Attach a 30-mL syringe with a stopcock.
  - h. Gently and slowly remove the fluid. Rapid withdrawal of pericardial fluid can result in shock or myocardial insufficiency.
  - i. Send fluid for appropriate laboratory studies (see Chapter 27).
  - j. In nonemergent conditions, this is best performed under two-dimensional echocardiographic guidance.
4. **A video on pericardiocentesis is available on the New England Journal of Medicine's website.**

### D. Paracentesis<sup>4</sup>

1. **Indications:** Percutaneous removal of intraperitoneal fluid for diagnostic or therapeutic purposes.
2. **Complications:** Bleeding, infection, puncture of viscera.
3. **Cautions:**
  - a. *Do not* remove a large amount of fluid too rapidly; hypovolemia and hypotension may result from rapid fluid shifts.
  - b. Avoid scars from previous surgery; localized bowel adhesions increase the chances of entering a viscus in these areas.
  - c. Urinary bladder should be empty to avoid perforation.
  - d. Never perform paracentesis through an area of cellulitis.

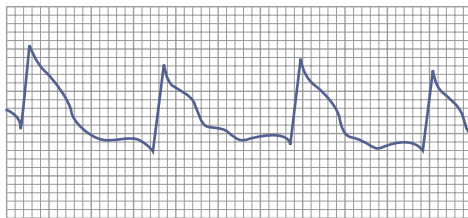


**FIGURE 3-15**

Subxiphoid approach for pericardiocentesis. **A**, Needle in pericardial sac with normal electrocardiogram (ECG). **B**, Needle in heart with current of injury pattern on ECG. (From Dieckmann R, Fiser D, Selbst S. Pediatric Emergency and Critical Care Procedures. St. Louis: Mosby, 1997.)



A (cont'd)



B (cont'd)

FIGURE 3-15, cont'd

**4. Procedure:**

- a. Prepare and drape abdomen as for a surgical procedure. Anesthetize puncture site.
  - b. With patient in semisupine, sitting, or lateral decubitus position, insert a 16G to 22G IV catheter attached to a syringe in midline 2 cm below umbilicus. In neonates, insert just lateral to rectus muscle in the right or left lower quadrants, a few centimeters above inguinal ligament.
  - c. Aiming cephalad, insert needle at a 45-degree angle while one hand pulls the skin caudally until entering the peritoneal cavity. This creates a Z tract when the skin is released and the needle removed. Apply continuous negative pressure.
  - d. Once fluid appears in the syringe, remove introducer needle and leave catheter in place. Attach a stopcock and aspirate slowly until an adequate amount of fluid has been obtained for studies or symptomatic relief.
  - e. If, on entering the peritoneal cavity, air is aspirated, withdraw the needle immediately. Aspirated air indicates entrance into a hollow viscus. (In general, penetration of a hollow viscus during paracentesis does not lead to complications.) Repeat paracentesis with sterile equipment.
  - f. Send fluid for appropriate laboratory studies (see Chapter 27).
5. **A video on paracentesis is available on the New England Journal of Medicine's website.**



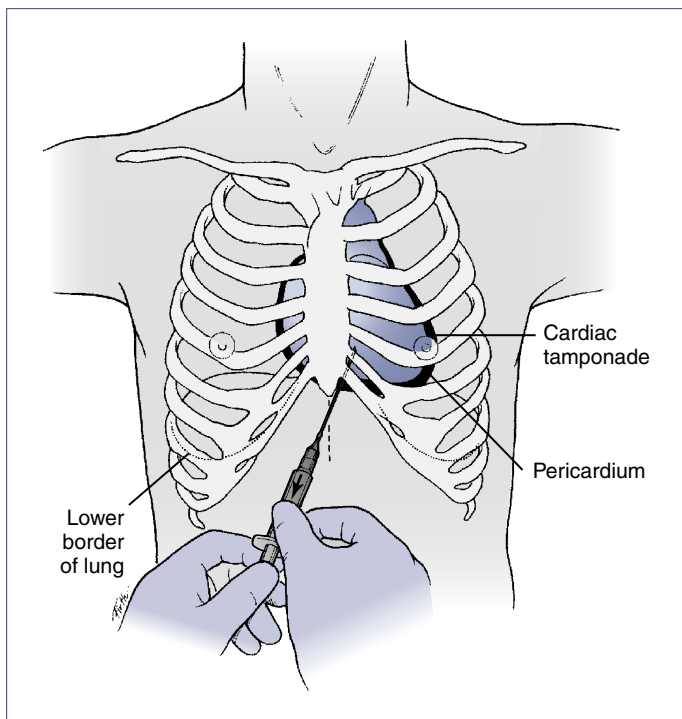


FIGURE 3-16

Insertion of needle for pericardiocentesis at junction of xiphoid and left costal margin, aiming toward left shoulder. (Modified from Brundage SI, Scott BG, Karmy-Jones R, et al. *Pericardiocentesis and pericardial window*. In: Shoemaker WC, Velmahos BC, Demetriadis D, eds. *Procedures and Monitoring for the Critically Ill*. Philadelphia: Saunders, 2002.)

### E. Urinary Bladder Catheterization<sup>4</sup>

1. **Indications:** To obtain urine for urinalysis and culture sterilely and to accurately monitor hydration status.
2. **Complications:** Hematuria, infection, trauma to urethra or bladder, intra-vesical knot of catheter (rarely occurs).
3. **Procedure:**
  - a. Infant/child should not have voided within 1 hour of procedure.  
**NOTE:** Catheterization is contraindicated in pelvic fractures, known trauma to the urethra, or blood at the meatus.
  - b. Prepare the urethral opening using sterile technique.
  - c. In males, apply gentle traction to the penis to straighten the urethra. In uncircumcised male infants, expose the meatus with gentle retraction of the foreskin. The foreskin has to be retracted only far enough to visualize the meatus.

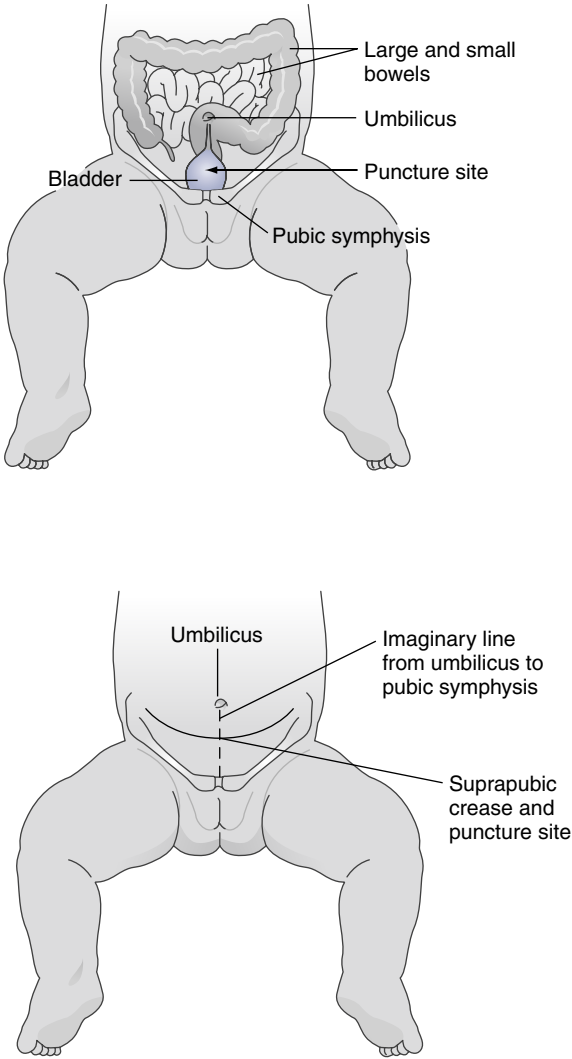
- d. Gently insert a lubricated catheter into the urethra. Slowly advance catheter until resistance is met at the external sphincter. Continued pressure will overcome this resistance, and the catheter will enter the bladder. In girls, the urethral orifice may be difficult to visualize, but it is usually immediately anterior to the vaginal orifice. Only a few centimeters of advancement is required to reach the bladder in girls. In boys, insert a few centimeters longer than the shaft of the penis.
- e. Carefully remove the catheter once specimen is obtained, and cleanse skin of iodine.
- f. If indwelling Foley catheter is inserted, inflate balloon with sterile water as indicated on bulb, then connect catheter to drainage tubing attached to urine drainage bag. Secure catheter tubing to inner thigh.
4. **A video on catheterization of the male urethra is available on the New England Journal of Medicine's website.**
5. **A video on catheterization of the female urethra is available on the New England Journal of Medicine's website.**

### F. Suprapubic Bladder Aspiration<sup>3</sup>

1. **Indications:** To sterilely obtain urine for urinalysis and culture in children younger than 2 years (avoid in children with genitourinary tract anomalies, coagulopathy, or intestinal obstruction). Bypasses distal urethra, thereby minimizing risk for contamination.
2. **Complications:** Infection (cellulitis), hematuria (usually microscopic), intestinal perforation.
3. **Procedure (Fig. 3-17):**
  - a. Anterior rectal pressure in girls or gentle penile pressure in boys may be used to prevent urination during the procedure. Child should not have voided within 1 hour of procedure.
  - b. Restrain infant in the supine, frog-leg position. Prepare suprapubic area in sterile fashion.
  - c. The site for puncture is 1 to 2 cm above the symphysis pubis in the midline. Use a syringe with a 22G, 1-inch needle, and puncture at a 10- to 20-degree angle to the perpendicular, aiming slightly caudad.
  - d. Gently exert suction as the needle is advanced until urine enters syringe. The needle should not be advanced more than 1 inch. Aspirate urine with gentle suction.
  - e. Cleanse skin of iodine.

### G. Soft Tissue Aspiration<sup>8</sup>

1. **Indications:** Cellulitis that is unresponsive to initial standard therapy, recurrent cellulitis or abscesses, immunocompromised patients in whom organism recovery is necessary and may affect antimicrobial therapy
2. **Complications:** Pain, infection, bleeding
3. **Procedure:**
  - a. Select site to aspirate at *point of maximal inflammation* (more likely to increase recovery of causative agent than leading edge of erythema or center).<sup>8</sup>
  - b. Cleanse area in sterile fashion.



**FIGURE 3-17**

Landmarks for suprapubic bladder aspiration. (From Dieckmann R, Fiser D, Selbst S. Pediatric Emergency and Critical Care Procedures. St. Louis: Mosby, 1997.)

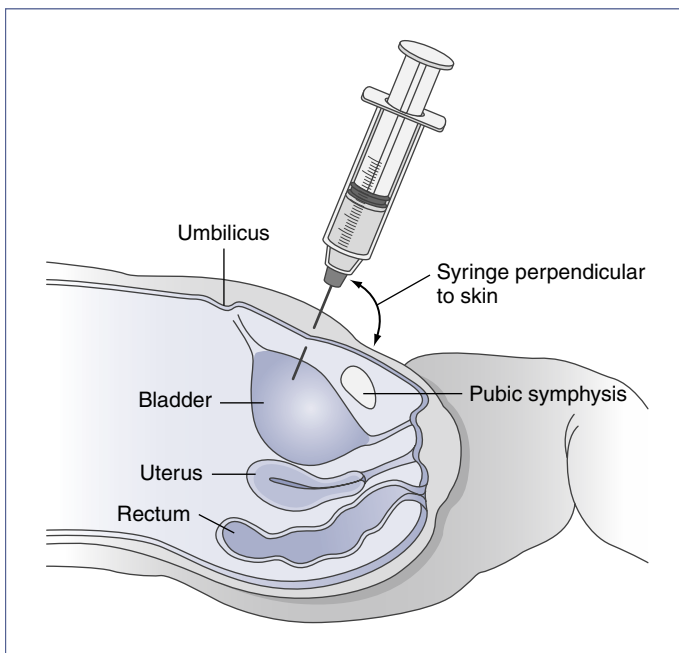


FIGURE 3-17, cont'd

- c. Local anesthesia with 1% lidocaine is optional.
- d. Fill tuberculin syringe with 0.1 to 0.2 mL of *nonbacteriostatic* sterile saline, and attach to needle.
- e. Using 18G or 20G needle (22G for facial cellulitis), advance to appropriate depth and apply negative pressure while withdrawing needle.
- f. Send fluid from aspiration for Gram stain and cultures. If no fluid is obtained, needle can be streaked on agar plate. Consider acid-fast bacillus (AFB) and fungal stains in immunocompromised patients.

## V. IMMUNIZATION AND MEDICATION ADMINISTRATION

### A. Subcutaneous Injections

1. **Indications:** Immunizations and other medications
2. **Complications:** Bleeding, infection, allergic reaction, lipohypertrophy or lipoatrophy after repeated injections
3. **Procedure:**
  - a. Locate injection site: Upper outer arm or outer aspect of upper thigh.
  - b. Cleanse skin with alcohol.
  - c. Insert 0.5-inch, 25G or 27G needle into subcutaneous layer at a 45-degree angle to the skin. Aspirate for blood, then inject medication.

**B. Intramuscular Injections**

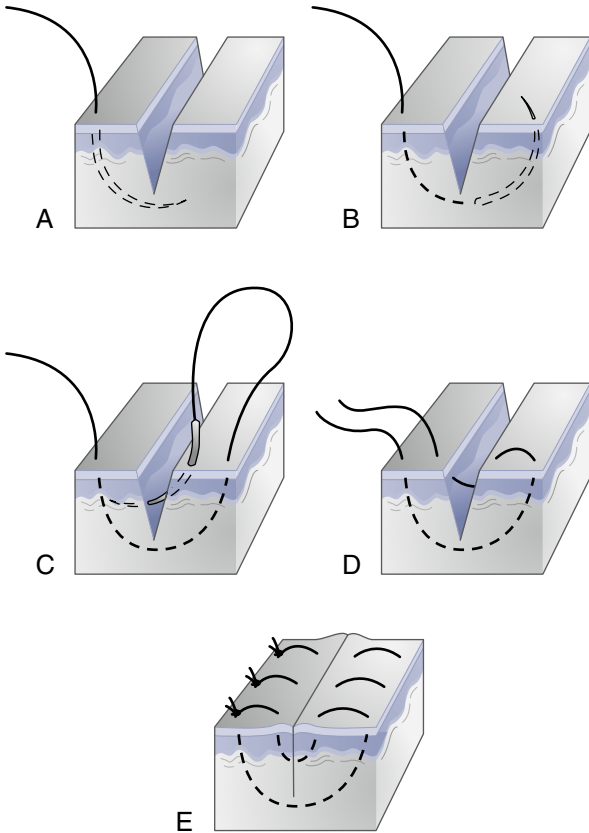
1. **Indications:** Immunizations and other medications
2. **Complications:** Bleeding, infection, allergic reaction, nerve injury
3. **Cautions:**
  - a. Avoid intramuscular (IM) injections in a child with a bleeding disorder or thrombocytopenia.
  - b. Maximum volume to be injected is 0.5 mL in a small infant, 1 mL in an older infant, 2 mL in a school-aged child, and 3 mL in an adolescent.
4. **Procedure:**
  - a. Locate injection site: Anterolateral upper thigh (vastus lateralis muscle) in smaller child or outer aspect of upper arm (deltoid) in older one. The dorsal gluteal region is less commonly used because of risk for nerve or vascular injury. To find the ventral gluteal site, form a triangle by placing your index finger on the anterior iliac spine and your middle finger on the most superior aspect of the iliac crest. The injection should occur in the middle of the triangle formed by the two fingers and the iliac crest.
  - b. Cleanse skin with alcohol.
  - c. Pinch muscle with free hand and insert 1-inch, 23G or 25G needle until hub is flush with skin surface. For deltoid and ventral gluteal muscles, needle should be perpendicular to skin. For anterolateral thigh, needle should be 45 degrees to the long axis of the thigh. Aspirate for blood, then inject medication.

**VI. BASIC LACERATION REPAIR****A. Suturing**

1. **Techniques (Fig. 3-18):**
  - a. Simple interrupted
  - b. Horizontal mattress: Provides eversion of wound edges
  - c. Vertical mattress: For added strength in areas of thick skin or areas of skin movement; provides eversion of wound edges
  - d. Running intradermal: For cosmetic closures
2. **Procedure:**

**NOTE:** Lacerations of the face, lips, hands, genitalia, mouth, or periorbital area may require consultation with a specialist. Ideally, lacerations at increased risk for infection (areas with poor blood supply, contaminated/crush injury) should be sutured within 6 hours of injury. Clean wounds in cosmetically important areas may be closed up to 24 hours after injury in the absence of significant contamination or devitalization. In general, bite wounds should not be sutured except in areas of high cosmetic importance (face). The longer sutures are left in place, the greater the scarring and potential for infection. Sutures in cosmetically sensitive areas should be removed as soon as possible. Sutures in high-tension areas (e.g., extensor surfaces) should stay in longer (Table 3-1).

  - a. Prepare child for procedure with appropriate sedation, analgesia, and restraint.

**FIGURE 3-18**

**A–E,** Vertical mattress suture. After initial placement of a simple interrupted stitch with a larger bite, make a backhand pass across the wound, taking small superficial bites. When knot is tied, edges of laceration should evert slightly. (From Dieckmann R, Fiser D, Selbst S. *Pediatric Emergency and Critical Care Procedures*. St. Louis: Mosby, 1997.)

- b. Anesthetize the wound with topical anesthetic or with lidocaine bicarbonate by injecting the anesthetic into the subcutaneous tissues (see Formulary).
- c. Forcefully irrigate the wound with copious amounts of sterile NS. Use at least 250 mL for smaller superficial wounds and more for larger wounds. This is the most important step in preventing infection. Avoid high-pressure irrigation of deep puncture wounds.

**TABLE 3-1**  
**GUIDELINES FOR SUTURE MATERIAL, SIZE, AND REMOVAL**

Body Region	Monofilament* (for Superficial Lacerations)	Absorbable† (for Deep Lacerations)	Duration (days)
Scalp	5-0 or 4-0	4-0	5-7
Face	6-0	5-0	3-5
Eyelid	7-0 or 6-0	—	3-5
Eyebrow	6-0 or 5-0	5-0	3-5
Trunk	5-0 or 4-0	3-0	5-7
Extremities	5-0 or 4-0	4-0	7-10
Joint surface	4-0	—	10-14
Hand	5-0	5-0	7
Foot sole	4-0 or 3-0	4-0	7-10

\*Examples of monofilament nonabsorbable sutures: Nylon, polypropylene. Good for the outermost layer of skin. Use 4-5 throws per knot. Polypropylene is good for scalp, eyebrows.

†Examples of absorbable sutures: Polyglycolic acid and polyglactin 910 (Vicryl). Good for deeper, subcuticular layers.

- d. Prepare and drape the patient for a sterile procedure.
  - e. Debride the wound when indicated. Probe for foreign bodies as indicated. Consider obtaining a radiograph if a radiopaque foreign body was involved in the injury.
  - f. Select suture type for percutaneous closure (see [Table 3-1](#)).
  - g. Match layers of injured tissues. Carefully match the depth of the bite taken on each side of the wound when suturing. Take equal bites from both wound edges. Apply slight thumb pressure on the wound edge as the needle is entering the opposite side. Pull the sutures to approximate wound edges, but not too tightly to avoid tissue necrosis. In delicate areas, sutures should be approximately 2 mm apart and 2 mm from the wound edge. Larger bites are acceptable where cosmesis is less important.<sup>3</sup>
  - h. When suturing is complete, apply topical antibiotic and sterile dressing. If laceration is in proximity of a joint, splinting of the affected area to limit mobility often speeds healing and prevents wound separation.
  - i. Check wounds at 48 to 72 hours in cases where wounds are of questionable viability, if wound was packed, or for patients prescribed prophylactic antibiotics. Change dressing at check.
  - j. For hand lacerations, close skin only; *do not* use subcutaneous stitches. Elevate and immobilize the hand. Consider consulting a hand or plastics specialist.
  - k. Consider the child's need for tetanus prophylaxis (see Chapter 16, Table 16-3, for guidelines).
3. **A video on basic laceration repair is available on the New England Journal of Medicine's website.**

## B. Skin Staples

### 1. Indications:

- a. Best for scalp, trunk, extremities
- b. More rapid application than sutures but can be more painful to remove
- c. Lower rates of wound infection

**2. Contraindications:**

- a. Not for areas that require meticulous cosmesis
- b. Avoid in patients who require magnetic resonance imaging (MRI) or CT

**3. Procedure:**

- a. Appose wound edges and staple.
- b. Left in place for the same length of time as sutures (see [Table 3-1](#)).
- c. To remove, use staple remover.

**C. Tissue Adhesives****1. Indications:**

- a. For use with superficial lacerations with clean edges
- b. Excellent cosmetic results, ease of application, and reduced patient anxiety
- c. Lower rates of wound infection

**2. Contraindications:**

- a. Not for use in areas under large amounts of tension (e.g., hands, joints).
- b. Use caution with areas near the eye.

**3. Procedure:**

- a. Use pressure to achieve hemostasis and clean the wound as explained previously.
- b. Hold together wound edges.
- c. Apply adhesive dropwise along the wound surface, avoiding applying adhesive to the inside of the wound. Hold in place for 20 to 30 seconds.
- d. If the wound is malaligned, remove the adhesive with forceps and reapply.
- e. Adhesive will slough off after 7 to 10 days.

**VII. MUSCULOSKELETAL PROCEDURES****A. Basic Splinting<sup>3</sup>**

- 1. **Indications:** to provide short-term stabilization of limb injuries

- 2. **Complications:** pressure sores, dermatitis, neurovascular impairment

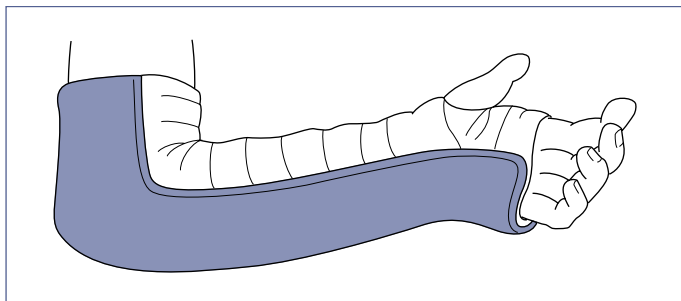
**3. Procedure:**

- a. Determine style of splint needed
- b. Measure and cut fiberglass or plaster to appropriate length. If using plaster, upper-extremity splints require 8 to 10 layers, and lower-extremity splints require 12 to 14 layers.
- c. Pad extremity with cotton Webril, taking care to overlap each turn by 50%. In prepackaged fiberglass splints, additional padding is not generally required. Bony prominences may require additional padding. Place cotton between digits if they are in a splint.
- d. Immerse plaster slabs into room-temperature water until bubbling stops. Smooth out wet plaster slab, avoiding any wrinkles.

*Warning:* Plaster becomes hot after drying.

- e. Position splint over extremity and wrap externally with gauze. When dry, an elastic wrap can be added.
- f. Alternatively, wet one side of fiberglass until saturated. Roll or fold to remove excess water. Mold splint as indicated.



**FIGURE 3-19**

Long arm posterior splint.

**NOTE:** Using warm water will decrease drying time. This may result in inadequate time to mold splint. Turn edge of the splint back on itself to produce a smooth surface. Take care to cover the sharp edges of fiberglass. When dry, wrap with elastic bandage.

- g. Use crutches or slings as indicated.
- h. The need for orthopedic referral should be individually assessed.

#### **B. Long Arm Posterior Splint (Fig. 3-19)**

1. **Indications:** Immobilization of elbow and forearm injuries

#### **C. Sugar Tong Forearm Splint (Fig. 3-20)**

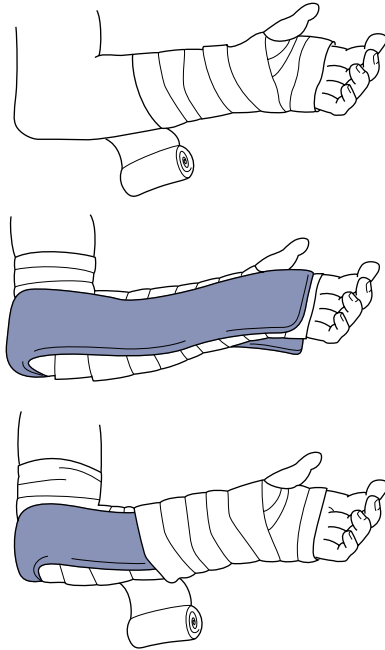
1. **Indications:** For distal radius and wrist fractures, to immobilize the elbow and minimize pronation and supination

#### **D. Ulnar Gutter Splint**

1. **Indications:** Nonrotated fourth or fifth (boxer) metacarpal metaphyseal fracture with less than 20 degrees of angulation, uncomplicated fourth and fifth phalangeal fracture.
2. **Assess for malrotation, displacement (especially Salter I-type fracture), angulation, and joint stability before splinting.**
3. **Procedure:** Elbow in neutral position, wrist in neutral position, metacarpophalangeal (MP) joint at 70 degrees, interphalangeal (IP) joint at 20 degrees. Apply splint in U shape from the tip of the fifth digit to 3 cm distal to the volar crease of the elbow. Splint should be wide enough to enclose the fourth and fifth digits.

#### **E. Thumb Spica Splint**

1. **Indications:** Nonrotated, nonangulated, nonarticular fractures of the thumb metacarpal or phalanx, ulnar collateral ligament injury (game-keeper's or skier's thumb), scaphoid fracture or suspected scaphoid fracture (pain in anatomic snuff box).
2. **Procedure:** Wrist in slight dorsiflexion, thumb in some flexion and abduction, IP joint in slight flexion. Apply splint in U shape from tip of thumb to mid-forearm. Mold the splint along the long axis of the thumb so that

**FIGURE 3-20**

Sugar tong forearm splint.

thumb position is maintained. This will result in a spiral configuration along the forearm.

#### **F. Volar Splint**

1. **Indications:** Wrist immobilization.
2. **Procedure:** Wrist in slight dorsiflexion. Apply splint on palmar surface from the MP joint to 2 to 3 cm distal to the volar crease of the elbow. It is useful to curve the splint to allow the MP joint to rest at an 80- to 90-degree angle.

#### **G. Posterior Ankle Splint**

1. **Indications:** Immobilization of ankle sprains and fractures of the foot, ankle, and distal fibula.
2. **Procedure:** Measure leg for appropriate length of plaster. Splint should extend to base of toes and upper portion of the calf. A sugar tong (stirrup) splint can be added to increase stability for ankle fractures.

## H. Radial Head Subluxation Reduction (Nursemaid's Elbow)

1. **Presentation:** Commonly occurs in children ages 1 to 4 years with a history of inability to use an arm after it was pulled. Child presents with affected arm held at the side in pronation, with elbow slightly flexed.
2. **Caution:** Rule out a fracture clinically before doing procedure. Consider radiograph if mechanism of injury or history is atypical.
3. **Procedure:**
  - a. Support the elbow with one hand, and place your thumb laterally over the radial head at the elbow. With your other hand, grasp the child's hand in a handshake position.
  - b. Quickly and deliberately supinate and externally rotate the forearm, and simultaneously flex the elbow. Alternatively, hyperpronation alone may be used. You may feel a click as reduction occurs.
  - c. Most children will begin to use the arm within 15 minutes, some immediately after reduction. If reduction occurs after a prolonged period of subluxation, it may take the child longer to recover use of the arm. In this case, the arm should be immobilized with a posterior splint.
  - d. If procedure is unsuccessful, consider obtaining a radiograph. Maneuver may be repeated if needed.
4. **A video guide for volar splints, ulnar gutter splints, thumb spica splints, long arm splints, sugar tong splints, and posterior ankle splints is available on the New England Journal of Medicine's website.**

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## Trauma, Burns, and Common Critical Care Emergencies

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 See additional content on Expert Consult

4

### I. TRAUMA: OVERVIEW

#### A. Primary Survey

The primary survey includes assessment of the ABCs (airway, breathing, circulation) via the algorithm **CAB: C**irculation, **A**irway, and **B**reathing.<sup>2</sup> See Chapter 1 for a complete algorithm.

**NOTE:** The CAB sequence is currently in use by the American Heart Association as part of the Pediatric Advanced Life Support (PALS) algorithm. The Advanced Trauma Life Support (ATLS) algorithm developed by the American College of Surgeons continues to support the ABC sequence in the primary survey. Depending on the patient and the injury incurred, either sequence may be used during acute trauma stabilization.

#### B. Secondary Survey

Procedures used in a secondary survey are listed in [Table 4-1](#) and include assessment of neurologic status using the quick screen **AVPU** (**A**lert, **V**ocal stimulation response, **P**ainful stimulation response, **U**nresponsive) or Glasgow Coma Scale (GCS). Remove all the patient's clothing, and perform a thorough head-to-toe examination. Remember to keep the child warm during the examination.

#### C. AMPLE History

Obtain an **AMPLE** history: **A**llergies, **M**edications, **P**ast illnesses, **L**ast meal, **E**vents preceding injury.

### II. SPECIFIC TRAUMATIC INJURIES

#### A. Minor Closed Head Trauma<sup>3</sup>

1. **Head injury can be caused by penetrating trauma, blunt force, rotational acceleration, or acceleration-deceleration injury.** Closed head trauma (CHT) can lead to depressed or nondepressed skull fracture, epidural or subdural hematoma, cerebral contusion, brain edema, increased intracranial pressure (ICP), brain herniation, concussion (mild to moderate diffuse brain injury), and/or coma (diffuse axonal injury [DAI]). See [Section III.B](#) for treatment of elevated ICP associated with severe CHT.
2. **Evaluation:**
  - a. Physical examination (after CAB and cervical spine [C-spine] immobilization):
    - (1) Assign GCS score (see Chapter 1).

**TABLE 4-1****SECONDARY SURVEY**

Organ System	Secondary Survey
Head	Scalp/skull injury Raccoon eyes: Periorbital ecchymoses; suggests orbital roof fracture Battle's sign: Ecchymoses behind pinna; suggests mastoid fracture Cerebrospinal fluid leak from ears/nose or hemotympanum suggests basilar skull fracture Pupil size, symmetry, and reactivity: Unilateral dilation of one pupil suggests compression of cranial nerve (CN) III and possible impending herniation; bilateral dilation of pupils is ominous and suggests bilateral CN III compression or severe anoxia and ischemia Corneal reflex Funduscopy examination for papilledema as evidence of increased intracranial pressure Hyphema
Neck	Cervical spine tenderness, deformity, injury Trachea midline Subcutaneous emphysema Hematoma Bruit
Chest	Clavicle deformity, tenderness Breath sounds, heart sounds Chest wall symmetry, paradoxical movement, rib deformity/fracture Petechiae over chest/head suggest traumatic asphyxia
Abdomen	Serial examinations to evaluate tenderness, distention, ecchymosis Shoulder pain suggests referred subdiaphragmatic process Orogastric aspirates with blood or bile suggest intraabdominal injury Splenic laceration suggested by left upper quadrant rib tenderness, flank pain, and/or flank ecchymoses "seatbelt sign"
Pelvis	Tenderness, symmetry, deformity, stability
Genitourinary	Laceration, ecchymoses, hematoma, bleeding Rectal tone, blood, displaced prostate Blood at urinary meatus suggests urethral injury; do not catheterize
Back	Log-roll patient to evaluate spine for step-off along spinal column Tenderness Open or penetrating wound
Extremities	Neurovascular status: Pulse, perfusion, pallor, paresthesias, paralysis, pain Deformity, crepitus, pain Motor/sensory examination Compartment syndrome: Pain out of proportion to expected; distal pallor/pulselessness
Neurologic	Quick screen: <b>A</b> lert, <b>V</b> ocal stimulation response, <b>P</b> ainful stimulation response, <b>U</b> nresponsive (AVPU) or Glasgow Coma Scale
Skin	Capillary refill, perfusion Lacerations, abrasions, contusion

## BOX 4-1

**CATCH CLINICAL DECISION RULE FOR DETERMINING WHETHER HEAD CT IS NEEDED IN THE SETTING OF MINOR CLOSED HEAD TRAUMA<sup>5</sup>**

If any one of the following findings in either category is present, obtain head CT.

**High risk (likely need for neurologic intervention):**

- GCS <15 at 2 hours after injury
- Suspected open or depressed skull fracture
- Worsening headache
- Irritability

**Medium risk (brain injury likely will be evident on CT):**

- Any sign of basal skull fracture (CSF leakage, hemotympanum, periorbital or mastoid ecchymosis)
- Large, boggy scalp hematoma
- Hazardous mechanism of injury (motor vehicle crash, fall from over 3 feet, fall down five or more stairs)

4

CSF, Cerebrospinal fluid; CT, computed tomography; GCS, Glasgow Coma Scale. Modified from CATCH: a clinical decision rule for the use of computed tomography in children with minor head injury. *CMAJ*. 2010;182:341-348.

- (2) Obtain vital signs; pay special attention to Cushing triad (hypertension, bradycardia, irregular respiratory pattern) as an indication of increased intracranial pressure.
  - (3) Perform neurologic examination as part of secondary survey (see [Table 4-1](#)).
  - (4) If severe symptoms or vital sign changes are present, or if major CHT, follow procedures for emergency management of increased ICP and coma (see [Section III.B](#)).
  - (5) Rule out possible drug or alcohol ingestion/use as etiology of altered mental status.
- b. Associated symptoms: Altered level or loss of consciousness (LOC), amnesia (before, during, or after the event), mental status change, behavior change, seizure activity, vomiting, headache, gait disturbance, visual change, or lethargy since event
  - c. Mechanism of injury:
    - (1) Linear forces: Less likely to cause LOC; more commonly lead to skull fractures, intracranial hematoma, or cerebral contusion.
    - (2) Rotational forces: Commonly cause LOC; occasionally associated with DAI.
    - (3) Suspect abuse if mechanism of injury is not consistent with sustained injuries.
3. **Management<sup>4</sup>:**
    - a. Evaluate C-spine (see [Section II.B](#)).
    - b. Consider if noncontrast computed tomography (CT) scan of head is indicated ([Box 4-1](#)).
      - (1) Most cases may be observed initially in the emergency department without neuroimaging.
      - (2) Vomiting or brief LOC is not an absolute indication for head CT.

- c. Observe patient:
  - (1) Monitor for 4 to 6 hours to detect delayed signs/symptoms of intracranial injury. A symptom-free lucid period can precede variable degrees of acute-onset mental status change with epidural bleeds.
  - (2) Recommend continued observation at home, and counsel parents on indications to have the patient reevaluated by medical staff. Continued observation can occur in the hospital if patient is clinically unstable or if there are concerns about home environment (caregiver reliability, follow-up, etc.).
- d. Consider hospitalizing patients with the following symptoms:
  - (1) Depressed or declining level of consciousness or prolonged unconsciousness (GCS 8–12)
  - (2) Focal neurologic deficit
  - (3) Increasing headache, persistent vomiting, or seizures
  - (4) Cerebrospinal fluid (CSF) otorrhea or rhinorrhea, hemotympanum, mastoid ecchymosis (Battle's sign), or periorbital ecchymosis (raccoon eyes)
  - (5) Linear skull fracture crossing the groove of the middle meningeal artery, a venous sinus of the dura, or the foramen magnum
  - (6) Depressed or compound skull fracture or fracture into the frontal sinus
  - (7) Bleeding disorder or patient on anticoagulation therapy
  - (8) Intoxication, illness, or injury obscuring neurologic state
  - (9) Suspected nonaccidental trauma
  - (10) Patient is unable to return to emergency department (ED) for reassessment
- e. Concussions in sports-related injuries<sup>6</sup>:
  - (1) Definition: Trauma-induced alteration of consciousness that may or may not cause LOC
  - (2) Immediate signs: Change in playing ability, confusion, slowing, memory disturbance (including of events surrounding injury), incoordination, headache, dizziness, nausea, vomiting, and LOC
  - (3) Postconcussive symptoms: Headaches, fatigue, sleep disturbance, nausea/vomiting, vision changes, tinnitus, balance problems, emotional/behavioral changes, sensitivity to light or sound, and cognitive changes
  - (4) Management: Evaluate CAB, perform mental status assessment
    - (a) Grade of concussion less important than carefully tracking recovery course over time
    - (b) Return to play only if: No signs or symptoms during rest or exertion, normal neurologic examination, neuroimaging normal (if obtained)
    - (c) Consider neuropsychologic testing if history of multiple injuries, recovery not progressing as expected
  - (5) Refer to Centers for Disease Control and Prevention Guidelines: Concussion in Youth Sports: <http://www.cdc.gov/concussion/HeadsUp/youth.html>

## B. Neck Injuries<sup>3</sup>

See Chapter 25 (Radiology) for in-depth evaluation of cervical trauma and reading C-spine films.

1. **Immobilize C-spine before history and physical examination.** Infants generally have large occiputs, so use support under neck/shoulders to maintain neutral position and avoid neck flexion. If patient is seen after immobilization by an emergency respondent, attempt to clear clinically and consider radiographic studies based on findings.
2. **Radiographic studies:**
  - a. Posteroanterior (PA), lateral views (including C7), and odontoid view
  - b. Flexion and extension views of C-spine can be considered if:
    - (1) Unstable C-spine injury not suspected.
    - (2) PA and lateral views are normal, but bony tenderness is present.
    - (3) Symptoms are present on palpation.
  - c. Magnetic resonance imaging (MRI) indicated to rule out direct spinal cord damage if neurologic symptoms persist and plain films are negative
3. **Clinically clear the C-spine:**
  - a. Patient must be awake, alert, and without a distracting injury or intoxication.
  - b. Palpate posterior neck for localized tenderness. If there is pain, maintain C-spine collar for immobilization until further evaluation can definitively rule out injury. If there is no pain, assess active and passive range of motion.

## C. Blunt Thoracic and Abdominal Trauma<sup>7</sup>

1. **Anatomic considerations in children:** Pliable rib cage, solid organs proportionally larger than those of adults, underdeveloped abdominal musculature
2. **Common injuries:**
  - a. Thoracic: Pneumothorax, hemothorax, pulmonary contusion, fractures, damage to major blood vessels, heart, or diaphragm
  - b. Abdominal: Damage to spleen, liver, kidneys, pancreas, genitourinary (GU) system, or major blood vessels; hematomas within the gastrointestinal (GI) tract
3. **Evaluation:**
  - a. Careful history and physical examination
  - b. Laboratory studies:
    - (1) Type and cross-match
    - (2) Thoracic injury: Complete blood cell count (CBC), pulse oximetry; consider arterial blood gas (ABG)
    - (3) Abdominal injury: CBC (follow serial hemoglobin values), electrolytes, liver function tests, amylase, lipase, urinalysis
  - c. Radiologic evaluation:
    - (1) Chest radiograph, with or without chest CT with intravenous (IV) contrast, if patient is stable.
    - (2) Abdominal CT with IV contrast if there is a concern based on history or physical examination (routine oral contrast *not* indicated; high false-negative rate for hollow viscus injury).



- (3) Consider focused abdominal ultrasound when coexisting injuries (e.g., neurologic or significant orthopedic) prevent CT scan.

#### 4. **Emergent treatment:**

- a. If significant trauma is suspected or diagnosed, consult a pediatric surgeon.
- b. Tension pneumothorax:
  - (1) Signs: Marked respiratory distress, distended neck veins, contralateral tracheal deviation, diminished breath sounds, compromised systemic perfusion, trauma arrest
  - (2) Treatment: Needle decompression, then chest tube placement directed toward lung apex (see Chapter 3)
- c. Open pneumothorax (also known as "sucking chest wound"): Allows free flow of air between atmosphere and hemithorax. Cover defect with occlusive dressing (i.e., petroleum jelly gauze), give positive-pressure ventilation, and insert chest tube (see Chapter 3).
- d. Hemothorax: Provide fluid resuscitation, followed by placement of a chest tube directed posteriorly and inferiorly.
- e. Abdominal trauma: Penetrating trauma requires surgical evaluation and exploration. Nonoperative management may be possible in blunt trauma, even in the presence of intraabdominal bleeding. Bleeding from injured spleen, kidneys, or liver is often self-limited. The decision to pursue operative vs. nonoperative management should be made by a surgeon.

#### **D. Orthopedic/Long Bone Trauma<sup>8,9</sup>**

- 1. **Fractures:** Some fracture patterns are unique to children (Fig. 4-1). Growthplate injuries are classified by the Salter-Harris classification (Table 4-2). Because ligaments are stronger than bones or growth plates in children, dislocations and sprains are relatively uncommon, whereas growth-plate disruption and bone avulsion are more common. For basic splinting techniques, see Chapter 3.
- 2. **Compartment syndrome<sup>1,9</sup>:** Elevated muscle compartment pressure (due to space limitation by surrounding fascia) impairs blood flow, resulting in nerve and muscle damage.
  - a. Common causes include crush injury, fractures (most common: tibia), burns, infections (necrotizing fasciitis), or hemorrhage.
  - b. Marked by **6 Ps**: **P**ain (earliest symptom), **P**aresthesias, **P**allor, **P**oikilothermia, **P**aralysis, **P**ulselessness.
    - (1) Unrelenting pain, even after appropriate analgesia, is the most sensitive sign.
    - (2) Pain with passive muscle stretch is a strong indicator.
  - c. Intercompartmental pressure measurement: Normal = 10 mmHg; symptoms occur with pressures 20 to 30 mmHg.
  - d. Management: Emergency fasciotomy within 6 hours of onset; absolutely indicated if pressure >30 mmHg.
  - e. Complications: Rhabdomyolysis. Follow urinalysis, creatine kinase (CK), electrolytes (risk for hyperkalemia). Consider saline resuscitation, urine alkalinization (with goal urine pH >6.5), or mannitol (0.25–0.5 g/kg).

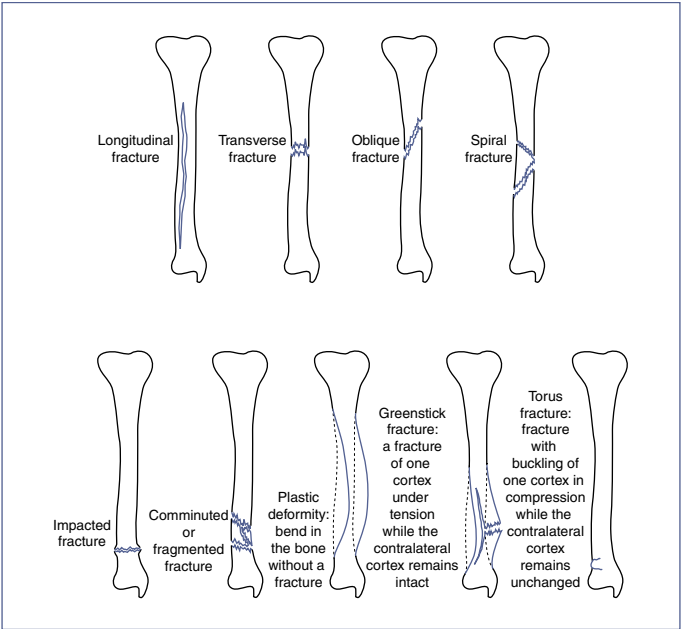


FIGURE 4-1

Fracture patterns unique to children. (Modified from Ogden JA. *Skeletal Injury in the Child*. 3rd ed. Philadelphia: WB Saunders, 2000.)

TABLE 4-2

SALTER-HARRIS CLASSIFICATION OF GROWTH PLATE INJURY				
Class I	Class II	Class III	Class IV	Class V
Fracture along growth plate	Fracture along growth plate with metaphyseal extension	Fracture along growth plate with epiphyseal extension	Fracture across growth plate, including metaphysis and epiphysis	Crush injury to growth plate without obvious fracture
I	II	III	IV	V

### III. COMMON CRITICAL CARE EMERGENCIES

#### A. Acute Hypertension<sup>10,11</sup>

##### 1. Assessment:

- a. Use appropriate cuff size for BP measurement. Ideal cuff should have a bladder length that is 80% of the patient's arm circumference and a bladder width that is at least 40% of the patient's arm circumference. Correlate with BP tables for age, height, and weight (Tables 7-1 and 7-2 and Figs. 7-2 and 7-3).
- b. Hypertensive *urgency*: Significant elevation in BP *without* accompanying end-organ damage; more common in children. Symptoms include headache, blurred vision, and nausea.
- c. Hypertensive *emergency*: Elevation of systolic and/or diastolic BP *with* acute end-organ damage (e.g., cerebral infarction or hemorrhage, pulmonary edema, renal failure, hypertensive encephalopathy, or seizures).
- d. Possible etiologies: Cardiovascular, renovascular, renal parenchymal, endocrine, central nervous system (CNS), medication, or ingestion.

**NOTE:** Rule out hypertension secondary to elevated ICP before lowering BP.

- e. Physical examination: Four-extremity BP, funduscopy (looking for papilledema, hemorrhage, exudate), visual acuity, thyroid examination, evidence of congestive heart failure (tachycardia, gallop rhythm, hepatomegaly, edema), abdominal examination (mass, bruit), thorough neurologic examination, evidence of virilization, cushingoid effect.
- f. Diagnostic evaluation:
  - (1) Initial: Urinalysis, blood urea nitrogen, creatinine, electrolytes, chest radiograph, electrocardiogram (ECG).
  - (2) Subsequent: Consider renin level, toxicology screen, thyroid and adrenal testing, urine catecholamines, abdominal ultrasound, renal Doppler ultrasound, head CT.

##### 2. Management: After elevated ICP is ruled out, do not delay treatment pending further diagnostic workup.

- a. Hypertensive emergency:
  - (1) Goal: Lower BP promptly but gradually to preserve cerebral autoregulation (Table 4-3).
    - (a) Mean arterial pressure (MAP) =  $1/3$  systolic +  $2/3$  diastolic BP
    - (b) Lower by  $1/3$  of planned MAP reduction over first 6 hours, *then*
    - (c) Lower by additional  $1/3$  over next 24 to 36 hours, *then*
    - (d) Lower final  $1/3$  over next 48 hours
  - (2) Consult nephrologist and/or cardiologist.
- b. Hypertensive urgency:
  - (1) Goal: To lower MAP by 20% over 1 hour and return to baseline levels over 24 to 48 hours (Table 4-4).
  - (2) Oral route may be adequate. Use of sublingual nifedipine is *not* recommended; a precipitous uncontrolled fall in BP may result.

**TABLE 4-3**  
**MEDICATIONS FOR HYPERTENSIVE EMERGENCY\***

Drug	Onset (Route)	Duration	Interval to Repeat	Comments
Diazoxide (arteriole vasodilator)	1–5 min (IV)	Variable (2–12 hr)	15–30 min	May cause edema, hyperglycemia
Hydralazine (arteriole vasodilator)	5–20 min (IV)	2–6 hr	4–6 hr	May cause reflex tachycardia, prolonged hypotension, nausea
<b>INFUSIONS</b>				
Nitroprusside (arteriole and venous vasodilator)	<30 sec (IV)	Very short	30–60 min	Requires ICU setting; follow thiocyanate level
Labetalol ( $\alpha$ -, $\beta$ -blocker)	1–5 min (IV)	Variable ( $\approx$ 6 hr)	10 min	May require ICU setting
Nicardipine (calcium channel blocker)	1 min (IV)	3 hr	15 min	May cause edema, headache, nausea, vomiting

\*See Formulary for dosing.  
ICU, Intensive care unit; IV, intravenous.

**TABLE 4-4**  
**MEDICATIONS FOR HYPERTENSIVE URGENCY\***

Drug	Onset (Route)	Duration	Interval to Repeat	Comments
Enalapril	15 min (IV)	12–24 hr	8–24 hr	May cause hyperkalemia, hypoglycemia
Minoxidil	30 min (PO)	2–5 days	4–8 hr	Contraindicated in pheochromocytoma

\*See Formulary for dosing.  
IV, Intravenous; PO, per os (oral).

### B. Increased Intracranial Pressure<sup>12,13,14</sup>

See Chapter 20 for evaluation and management of hydrocephalus.

#### 1. Assessment:

- Obtain history regarding trauma, prior shunt or other neurologic surgical or medical condition, vomiting, fever, headache, neck pain, unsteadiness, seizure, vision change, gaze preference, and change in mental status. In infants, look for irritability, vomiting, poor feeding, lethargy, and bulging fontanelle.
- Physical examination:
  - Evaluate vital signs for Cushing triad (hypertension, bradycardia, irregular respiratory pattern) as a sign of increasing intracranial pressure.
  - Thorough neurologic examination: Attention to photophobia, pupillary response, papilledema, cranial nerve dysfunction (especially

paralysis of upward gaze or abduction), neck stiffness, neurologic deficit, abnormal posturing, altered mental status, or evidence of trauma.

- c. Laboratory studies: CBC, electrolytes, glucose, toxicology screen, blood culture. Lumbar puncture (LP) is contraindicated due to herniation risk if cause is obstructive.
2. **Management:** Elevate head of bed 30 degrees. Patient should be mid-line with neck straight to maximize venous drainage from the head. Keep life-saving stabilizing devices in place, but be certain cervical collars and medical devices do not obstruct jugular venous drainage. Obtain emergent neurosurgical consult and head CT. Do not lower BP if elevated ICP is suspected. Immobilize C-spine if trauma is suspected.
  - a. Stable patient (responsive, stable vital signs, no focal findings): Apply cardiorespiratory monitor.
  - b. Unstable patient:
    - (1) Give normal saline or hyperosmolar solutions for maintenance fluids.
    - (2) For temporary reduction of ICP give 3% NaCl bolus (range, 2 to 5 mL/kg). Maintain serum osmolarity goal of <360 mOsm/L.
      - (a) Alternatively, can use mannitol 0.25 g/kg with max single dose of 12.5 g. Can increase dose to 1 g/kg, although high dose mannitol can produce significant hypotension due to osmotic diuresis, so consider giving fluid bolus at same time. If using mannitol, remember to place a Foley catheter.
    - (3) Reserve hyperventilation for acute management; keep partial pressure of carbon dioxide ( $P_{aCO_2}$ ) at 30 to 35 mmHg. Provide controlled neuroprotective intubation as outlined in Table 1-1, and consider advanced neuromonitoring for evaluation of cerebral ischemia.
    - (4) In traumatic brain injury (TBI), consider controlled moderate hypothermia (32° to 33°C).
  - c. Do not delay antibiotics if meningitis suspected.
  - d. In space-occupying lesions (tumors, abscesses), consider dexamethasone to reduce cerebral edema (in consultation with a neurosurgeon). Otherwise, corticosteroids are not recommended for children with TBI.
  - e. Consider epinephrine or phenylephrine infusion to maintain systemic pressure above ICP.

$$\text{Cerebral perfusion pressure (CPP)} = \text{MAP} - \text{ICP}$$

Goal minimum CPP is 40 mmHg in children with TBI.

- f. Prevent hyperthermia: Goal is body temperature <37.5°C.
- g. Consider consult for prophylactic seizure control to reduce incidence of early posttraumatic seizures in children with TBI.
- h. Avoid hypotension, hypoxia, hypercarbia, and hypovolemia.

### C. Shock<sup>15,16</sup>

1. **Definition:** Physiologic state characterized by inadequate oxygen and nutrient delivery to meet tissue demands. See [Table 4-5](#) for categorization.
- a. Compensated shock: Body maintains perfusion to vital organs. This clinical state may be hard to detect because BP changes are a late finding in young children. Tachycardia may be present and is often the most sensitive vital sign change.
- b. Decompensated shock: Poor perfusion, tachycardia, hypotension.
2. **Causes (see [Table EC 4-A](#)):**
  - a. Hypovolemic shock.
  - b. Distributive shock (including septic, anaphylactic, and neurogenic shock).
  - c. Cardiogenic shock.
  - d. Obstructive shock (including cardiac tamponade, tension pneumothorax, massive pulmonary embolism).
3. **Management ([Fig. 4-2](#)):** Always treat underlying cause.

### D. Respiratory Failure<sup>15</sup>

1. **Definition:** Failure of the lungs to exchange oxygen and/or carbon dioxide
2. **Causes:**
  - a. Neurologic: Muscle weakness, altered sensorium, CNS impairment
  - b. Obstruction: Foreign body, inflammation
  - c. Parenchymal disease: Pneumonia, pulmonary edema, acute respiratory distress syndrome (ARDS), asthma
  - d. Mechanical: Abnormal chest wall, trauma
3. **Management:**
  - a. Noninvasive positive-pressure ventilation
  - b. Intubation and mechanical ventilation (see Chapter 1 for discussion of intubation)
4. **Types of ventilatory support:**
  - a. Volume limited:
    - (1) Delivers a preset tidal volume to a patient, regardless of pressure required
    - (2) Risk for barotrauma reduced by pressure alarms and pressure pop-off valves that limit peak inspiratory pressure (PIP)
  - b. Pressure limited:
    - (1) Gas flow is delivered to the patient until a preset pressure is reached and then held for the set inspiratory time (reduces the risk for barotrauma).
    - (2) Useful for neonatal and infant ventilatory support (<10 kg), where the volume of gas being delivered is small in relation to the volume of compressible air in the ventilator circuit, which makes reliable delivery of a set tidal volume difficult.
  - c. High-frequency ventilation  
[See additional content on Expert Consult.<sup>17</sup>](#)
5. **Ventilator parameters:**
  - a. PIP: Peak pressure attained during the respiratory cycle
  - b. Positive end-expiratory pressure (PEEP): Airway pressure maintained between inspiratory and expiratory phases; prevents alveolar collapse during expiration, decreases work of reinflation, and improves gas exchange

TABLE EC 4-A					
TYPES OF SHOCK, PHYSIOLOGIC RESPONSE, AND BASIC TREATMENT					
Type of Shock	HR	Preload	Contractility	SVR	Treatment
Hypovolemic	↑	↓↓	+/-	↑	<ul style="list-style-type: none"><li>• High-flow oxygen</li><li>• Fluid resuscitation: Evaluate perfusion after 60 mL/kg total volume bolused, then consider pressors</li></ul>
Septic (early, warm)	↑	↓↓	+/-	↓	<ul style="list-style-type: none"><li>• High-flow oxygen</li><li>• Fluid resuscitation</li><li>• Antibiotics</li><li>• Pressors (dopamine, norepinephrine, phenylephrine)</li></ul>
Septic (late, cold)	↑	↓↓	↓	↑	<ul style="list-style-type: none"><li>• High-flow oxygen</li><li>• Fluid resuscitation</li><li>• Antibiotics</li><li>• Pressors (dopamine, epinephrine, phenylephrine)</li></ul>
Anaphylactic	↑	↓↓	↓	↓	<ul style="list-style-type: none"><li>• High-flow oxygen</li><li>• Epinephrine (IM)</li><li>• Fluid resuscitation</li></ul>
Neurogenic	↑	↓↓	+/-	↓↓	<ul style="list-style-type: none"><li>• Fluid resuscitation</li><li>• Pressors (norepinephrine)</li></ul>
Cardiogenic	↑	↑	↓↓	↑	<ul style="list-style-type: none"><li>• High-flow oxygen</li><li>• Fluid resuscitation (5–10 mL/kg)</li><li>• CHF management (CPAP/BiPAP, diuretics, ACE inhibitors)</li><li>• Inotropes (milrinone, dobutamine)</li></ul>
Obstructive	Cause dependent	Cause dependent	Cause dependent	Cause dependent	<ul style="list-style-type: none"><li>• Therapy directed at primary etiology of shock</li></ul>

ACE, Angiotensin-converting enzyme; BiPAP, bilevel positive airway pressure; CHF, congestive heart failure; CPAP, continuous positive airway pressure; HR, heart rate; IM, intramuscular; SVR, systemic vascular resistance.

- (1) High-frequency oscillatory ventilation (HFOV):
  - (a) High-amplitude and high-frequency pressure waveform generated in the ventilator circuit. Tidal volumes are less than dead space. Bias gas flow provides fresh gas at ventilator and maintains airway pressure.
  - (b) Minimizes barotrauma and oxygen toxicities.
  - (c) Patient must be euvolemic (owing to risk for decreased venous return).
- (2) High-frequency jet ventilation:
  - (a) Used simultaneously with a conventional ventilator.
  - (b) A jet injector port delivers short bursts of inspiratory gas.
  - (c) Adequate gas exchange can be achieved at low airway pressures, providing maintenance of lung volume and minimal risk for barotrauma.



TABLE 4-5

CATEGORIZATION OF HEMORRHAGE AND SHOCK IN PEDIATRIC TRAUMA PATIENTS<sup>22,23</sup>

System	Class I: Compensated Shock, Very Mild Hemorrhage (<15% Blood Volume Loss)	Class II: Compensated Shock, Mild Hemorrhage (15%–30% Blood Volume Loss)	Class III: Decompensated Shock, Moderate Hemorrhage (30%–40% Blood Volume Loss)	Class IV: Cardiopulmonary Failure, Severe Hemorrhage (>40% Blood Volume Loss)
<b>Cardiovascular</b>	Normal heart rate Normal peripheral pulses Strong central pulses Normotension to slight hypertension No acidosis	Mild tachycardia Normal or weak peripheral pulses Strong central pulses Normotension to slight hypotension	Moderate tachycardia Weak or absent peripheral pulses Weak central pulses Frank hypotension	Severe tachycardia Absent peripheral pulses Weak or absent central pulses Profound hypotension
<b>Respiratory</b>	Normal respiratory rate	Mild tachypnea	Moderate tachypnea	Severe tachypnea, bradypnea, or apnea
<b>Neurologic</b>	Slight anxiety	Mild anxiety, confusion, combative	Severe anxiety, confusion, lethargy	Severe confusion, obtundation, lethargy, comatose
<b>Integumentary</b>	Warm extremities, pink  Normal capillary refill (<2 sec)	Cool extremities, mottling  Poor capillary refill (>2 sec)	Cool extremities, mottling, or pallor  Delayed capillary refill (>3 sec)	Cold extremities, pallor, or cyanosis Prolonged capillary refill (>5 sec)
<b>Excretory</b>	Normal urine output	Mild oliguria, increased specific gravity	Marked oliguria, increased blood urea nitrogen	Severe oliguria or anuria

Modified from Fleisher GR, Ludwig S, ed. *Textbook of Pediatric Emergency Medicine*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2006.

**Initial management:**

- Early recognition based on vital sign and physical examination changes is key
- Establish access via large-bore IV or IO
- Start high-flow oxygen via facemask or nasal cannula, even in the absence of respiratory distress

**First 5–15 minutes:**

- Rapidly push 20 mL/kg isotonic saline or colloid
  - Each 20 mL/kg should be given in 5 minutes or less
  - Many patients require total of 60 mL/kg, some may require up to 200 mL/kg within the first hour of shock
  - Continue until perfusion improves or signs of fluid overload such as pulmonary crackles or hepatomegaly develop
- Correct hypoglycemia and hypocalcemia
- Start broad-spectrum IV antibiotics

**At 15 minutes without reversal of shock:**

- Start inotrope via second IV/IO access site
  - Cold shock—dopamine 2 to 20 mcg/kg/min or epinephrine 0.05 to 1 mcg/kg/min
  - Warm shock—norepinephrine 0.05 to 2 mcg/kg/min
- Consider securing airway with early intubation and mechanical ventilation

**At 60 minutes without reversal of shock:**

- Give hydrocortisone 2 mg/kg (max 100 mg) in patients at risk for adrenal insufficiency or patients who are unresponsive to pressors
- Consider transfer to pediatric intensive care unit

**Note:**

It is very important to prepare for each step in advance to be able to complete the recommended interventions within the first hour of recognized shock.

**FIGURE 4-2**

Emergency management of pediatric shock—first hour. (From Brierley J, Carcillo JA, Choong K, et al. *Clinical practice parameters for hemodynamic support of pediatric and neonatal septic shock: 2007 update from The American College of Critical Care Medicine*. Crit Care Med. 2009;37:666-688.)

- c. Rate (intermittent mandatory ventilation) or frequency (Hz): Number of mechanical breaths delivered per minute, or rate of oscillations in HFOV
- d. Inspired oxygen concentration ( $\text{FiO}_2$ ): Fraction of oxygen present in inspired gas
- e. Inspiratory time ( $\text{Ti}$ ): Length of time spent in the inspiratory phase of the respiratory cycle
- f. Tidal volume ( $\text{V}_\text{T}$ ): Volume of gas delivered during inspiration
- g. Power ( $\Delta\text{P}$ ): Amplitude of the pressure waveform in HFOV
- h. Mean airway pressure ( $\overline{\text{PAW}}$ ): Average pressure over entire respiratory cycle

#### **6. Modes of operation:**

- a. Intermittent mandatory ventilation (IMV): A preset number of breaths are delivered each minute. Patient can take breaths on his or her own, but the ventilator may cycle on during a patient breath.
- b. Synchronized IMV (SIMV): Similar to IMV, but the ventilator synchronizes delivered breaths with inspiratory effort and allows the patient to finish expiration before cycling on. More comfortable for patient than IMV.
- c. Assist control ventilation (AC): Every inspiratory effort by the patient triggers a ventilator-delivered breath at the set  $\text{V}_\text{T}$ . Ventilator-initiated breaths are delivered when the spontaneous rate falls below the backup rate.
- d. Pressure support ventilation (PSV): Inspiratory effort opens a valve, allowing airflow at a preset positive pressure. Patient determines rate and inspiratory time. May be used in combination with other modes of operation. Determine effectiveness of ventilation by monitoring tidal volumes.
- e. Noninvasive positive-pressure ventilation (NIPPV): Respiratory support provided through face mask.
  - (1) Continuous positive airway pressure (CPAP): Delivers airflow (with set  $\text{FiO}_2$ ) to maintain a set airway pressure
  - (2) Bilevel positive airway pressure (BiPAP): Delivers airflow to maintain set pressures for inspiration and expiration

#### **7. Initial ventilator settings:**

- a. Volume limited:
  - (1) Rate: Approximately normal range for age (see Table 24-1).
  - (2)  $\text{V}_\text{T}$ : Approximately 8 to 10 mL/kg.
  - (3)  $\text{Ti}$ : Generally use inspiration-to-expiration (I/E) ratio of 1:2. More prolonged expiratory phases are required for obstructive diseases to avoid air trapping.
  - (4)  $\text{FiO}_2$ : Selected to maintain targeted oxygen saturation and partial pressure of arterial oxygen ( $\text{PaO}_2$ ).
- b. Pressure limited:
  - (1) Rate: Approximately normal range for age (see Table 24-1).
  - (2) PEEP: Start with 3 to 5 cm  $\text{H}_2\text{O}$  and increase as clinically indicated. Monitor for decreases in cardiac output with increasing PEEP.
  - (3) PIP: Set at pressure required to produce adequate chest wall movement (approximate this using hand-ventilating and manometry).
  - (4)  $\text{FiO}_2$ : Selected to maintain targeted oxygen saturation and  $\text{PaO}_2$ .

c. HFOV

See additional content on Expert Consult.

**8. Further ventilator management:**

- a. Follow patient closely with pulse oximetry, end-tidal carbon dioxide measurements, and clinical assessment. Confirm findings with ABGs, and adjust ventilator parameters as indicated (Table 4-6).
- b. In cases of ARDS or other condition of poor compliance or air leaks, permissive hypercapnia and  $V_T$  of 5 mL/kg should be used to avoid barotrauma.
- c. Parameters for initiating high-frequency ventilation:
  - (1) Oxygenation index (OI) >40 (see Section III.G for calculation of OI)
  - (2) Inability to provide adequate oxygenation or ventilation with conventional ventilator
- d. Parameters predictive of successful extubation:
  - (1)  $Paco_2$  appropriate for patient
  - (2) PIP generally 14 to 16 cm H<sub>2</sub>O
  - (3) PEEP 2 to 3 cm H<sub>2</sub>O (infants) or 5 cm H<sub>2</sub>O (children)
  - (4) IMV 2 to 4 breaths/min (infants); children may be weaned to CPAP or pressure support
  - (5)  $Fio_2$  <40% (maintaining  $Pao_2$  >70)
  - (6) Adequate air leak around endotracheal tube in cases of airway edema or stenosis
  - (7) Maximum negative inspiratory pressure (NIF) >20 to 25 cm H<sub>2</sub>O
  - (8) Minimal secretions

**E. Status Epilepticus (See Chapter 1)**

**F. Status Asthmaticus (See Chapter 1)**

**G. Critical Care Reference Data**

**1. Minute ventilation ( $V_E$ ):**

$$V_E = \text{Respiratory rate} \times \text{Tidal volume } (V_T)$$

- a.  $V_E \times Paco_2 = \text{constant}$  (for volume-limited ventilation)
- b. Normal  $V_T = 8$  to 10 mL/kg

**TABLE 4-6**  
**EFFECTS OF VENTILATOR SETTING CHANGES**

Ventilator Setting Changes	Typical Effects on Blood Gases	
	$Paco_2$	$Pao_2$
↑ PIP	↓	↑
↑ PEEP	↑	↑
↑ Rate (IMV)	↓	Minimal ↑
↑ I:E ratio	No change	↑
↑ $Fio_2$	No change	↑
↑ Flow	Minimal ↓	Minimal ↑
↑ Power (in HFOV)	↓	No change
↑ PAW (in HFOV)	Minimal ↓	↑

$Fio_2$ , Fraction of inspired oxygen; HFOV, high-frequency oscillatory ventilation; I:E, inspiratory/expiratory ratio; IMV, intermittent mechanical ventilation;  $Pao_2$ , partial pressure of arterial oxygen;  $Paco_2$ , partial pressure of carbon dioxide; PAW, mean airway pressure; PEEP, positive end-expiratory pressure; PIP, peak inspiratory pressure.

- (1) Frequency: 10 to 15 Hz for neonates, 5 to 8 Hz for children.
  - (2) Power: Select to achieve adequate chest wall movement.
  - (3) Mean airway pressure: 1 to 4 cm H<sub>2</sub>O higher than settings on a conventional ventilator.
  - (4) Fio<sub>2</sub>: Selected to maintain targeted oxygen saturation and Pao<sub>2</sub>.
- d. High-frequency jet ventilator:
- (1) PIP: Increase 2 cm H<sub>2</sub>O over conventional ventilator setting.
  - (2) Ti: Set at 0.02 seconds.
  - (3) Frequency: In neonates, set at 420 cycles/sec.

**2. Alveolar gas equation:**

$$PAO_2 = P_{iO_2} - (P_{aCO_2}/R)$$

$$P_{iO_2} = F_{iO_2} \times (P_B - 47 \text{ mmHg})$$

- $P_{iO_2}$  = partial pressure of inspired  $O_2$  minus 150 mmHg at sea level on room air.
- R = respiratory exchange quotient ( $CO_2$  produced/ $O_2$  consumed) = 0.8.
- $P_{aCO_2}$  = partial pressure of alveolar  $CO_2$  minus partial pressure of arterial  $CO_2$  ( $P_{aCO_2}$ ).
- $P_B$  = atmospheric pressure = 760 mmHg at sea level. Adjust for high-altitude environment.
- Water vapor pressure = 47 mmHg.
- $PAO_2$  = partial pressure of  $O_2$  in the alveoli.

**3. Alveolar-arterial oxygen gradient (A-a gradient):**

$$A - a \text{ gradient} = PAO_2 - Pao_2$$

- Obtain ABG, measuring  $Pao_2$  and  $P_{aCO_2}$  with patient on 100%  $F_{iO_2}$  for at least 15 minutes.
  - Calculate the  $PAO_2$  and then the A-a gradient.
  - The larger the gradient, the more serious the respiratory compromise. A normal gradient is 20 to 65 mmHg on 100%  $O_2$  or 5 to 20 mmHg on room air.
- 4. Oxygenation Index (OI):**

$$OI = \frac{\text{Mean airway pressure (cm H}_2\text{O)} \times F_{iO_2} \times 100}{Pao_2}$$

OI >35 for 5 to 6 hours is one criterion for ECMO (extracorporeal membrane oxygen) support.

See more critical care reference data on Expert Consult.

## IV. ANIMAL BITES 3.18

**A. Wound Considerations**

- High infection risk:** Puncture wounds, crush injury, bites over hand, foot, genitalia, or joint surface, bites from a cat or human, wounds in asplenic or immunocompromised patients, wounds with care delayed >12 hours
- Special considerations:**
  - Deep bites: Possibility of foreign body or fracture—consider radiographs (especially hand or scalp)
  - Periorbital bites: Possibility of corneal abrasion, lacrimal duct involvement, or other ocular damage—consider ophthalmologic evaluation
  - Hand: Site most prone to infection—follow for development of osteomyelitis
  - Nose: Evaluate for cartilage injury

5. **Oxygen Content ( $\text{CaO}_2$ )**

$\text{O}_2$  content of sample (mL/dL) = ( $\text{O}_2$  capacity  $\times$   $\text{O}_2$  saturation [as decimal])  
+ dissolved  $\text{O}_2$

- $\text{O}_2$  capacity = hemoglobin (g/dL)  $\times$  1.34
- Dissolved  $\text{O}_2$  =  $\text{PaO}_2$  (of sample)  $\times$  0.003
- Hemoglobin carries more than 99% of  $\text{O}_2$  in blood under standard conditions.

6. **Arteriovenous  $\text{O}_2$  Difference ( $\text{AVDO}_2$ )**

$\text{AVDO}_2 = \text{CaO}_2 - \text{CvO}_2 = \text{Arterial } \text{O}_2 \text{ content} - \text{Mixed venous } \text{O}_2 \text{ content}$

- Usually done after placing patient on 100%  $\text{FiO}_2$  for 15 minutes.
- Obtain ABG and mixed venous blood sample (best obtained from pulmonary artery catheter), and measure  $\text{O}_2$  saturation in each sample.
- Calculate arterial and mixed venous oxygen contents and then  $\text{AVDO}_2$  (normal, 5 mL/100 dL).
- Used in calculating  $\text{O}_2$  extraction ratio (see next point).

7.  **$\text{O}_2$  Extraction Ratio**

$$\text{O}_2 \text{ extraction} = (\text{AVDO}_2 / \text{CaO}_2) \times 100$$

Normal range, 28% to 33%

- Calculate  $\text{AVDO}_2$  and  $\text{O}_2$  contents.
- Extraction ratios are indicative of adequacy of  $\text{O}_2$  delivery to tissues, with increasing extraction ratios suggesting that metabolic needs may be outpacing oxygen content being delivered.  
(From Mesiano G, Davis GM. Ventilatory strategies in the neonatal and paediatric intensive care units. *Paediatr Respir Rev.* 2008;9: 281-288.)

8. **Intrapulmonary Shunt Fraction ( $\text{Qs}/\text{Qt}$ )**

$$\frac{\text{Qs}}{\text{Qt}} = \frac{(\text{A} - \text{a gradient}) \times 0.003}{\text{AVDO}_2 + (\text{A} - \text{a gradient}) \times 0.003}$$

where  $\text{Qt}$  is cardiac output and  $\text{Qs}$  is flow across right-to-left shunt

- Formula assumes ABGs obtained on 100%  $\text{FiO}_2$ .
- Represents the mismatch of ventilation and perfusion and is normally <5%.
- A rising shunt fraction (usually >15% to 20%) is indicative of progressive respiratory failure.

3. Animal species (Table 4-7)

B. Management

1. Wound hygiene:

- a. Irrigate with copious amounts (at least 100 mL/cm of laceration) of sterile saline using high-pressure syringe irrigation. Do not irrigate puncture wounds. Do not soak the wound. Do not use alcohol or peroxide to clean.
- b. Debride devitalized tissue and evaluate for foreign bodies.
- c. Consider surgical debridement/exploration for extensive wounds, wounds involving metacarpophalangeal joint, and cranial bites by a large animal.
- d. Culture only if evidence of infection is present.

2. Closure:

- a. Avoid closing wounds of high infection risk (see Section IV.A). Exception: Cat bites on the face or scalp may be closed.
- b. Wounds that involve tendons, joints, deep fascia, or major vasculature should be evaluated by a plastic or hand surgeon and, if indicated, closed in the operating room.
- c. Suturing: When indicated, closure should be done with minimal simple interrupted nylon sutures that are as superficial as possible. Loosely approximate wound edges. Use prophylactic antibiotics.
  - (1) Head and neck: Can usually be safely sutured (with exceptions noted) after copious irrigation and wound debridement if within 6 to 8 hours of injury and no signs of infection. Facial wounds often require primary closure for cosmetic reasons; good vascular supply lowers infection risk.

TABLE 4-7  
ANIMAL BITES

Animal	Common Organism(s)	Special Considerations
Dog	<i>Staphylococcus aureus</i> <i>Pasteurella multocida</i> <i>Streptococcus</i> spp. <i>Capnocytophaga canimorsus</i> Anaerobes	Crush injury
Cat	<i>Pasteurella multocida</i> <i>Staphylococcus aureus</i> <i>Moraxella catarrhalis</i> <i>Bartonella henselae</i>	Deep puncture wound Often associated with fulminant infection, abscess, and/or osteomyelitis Slow to respond to treatment
Human	<i>Streptococcus viridans</i> <i>Staphylococcus aureus</i> Anaerobes <i>Eikenella corrodens</i> Hepatitis B and C HIV (rare, associated with blood in biter's saliva)	Consider child abuse, especially if intercanine distance >3 cm High infection and complication rate
Rodent	<i>Streptobacillus moniliformis</i> <i>Spirillum minus</i>	Low incidence of secondary infection Rat-bite fever—occurs rarely



- (2) **Hands:** In large wounds, subcutaneous dead space should be closed with minimal absorbable sutures, with delayed cutaneous closure in 3 to 5 days if there is no evidence of infection.
- 3. **Antibiotics:** Prophylactic antibiotics are indicated in cases of high infection risk, as listed in Section IV.A. See Chapter 17 for appropriate antibiotic therapies and treatment course.
- 4. **Rabies and tetanus prophylaxis:** Always give postexposure prophylaxis when animal is a skunk, raccoon, bat, fox, woodchuck, or other carnivore. For other cases, see Chapter 16.
- 5. **Imaging:** Obtain if bite is extensive, on the hand or closed fist, and after a "mauling" injury. Imaging can reveal fracture, air in joint space, or a foreign body in the wound.
- 6. **Disposition:**
  - a. Outpatient care: Obtain careful follow-up of all bite wounds within 24 to 48 hours, especially those requiring surgical closure. Extremity wounds, especially of the hands, should be immobilized in position of function and kept elevated. Wounds should be kept clean and dry.
  - b. Inpatient care: Consider hospitalization for observation and parenteral antibiotics for significant human bites, immunocompromised or asplenic hosts, deep or severe infections, bites associated with systemic complaints, bites with significant functional or cosmetic morbidity, and/or unreliable follow-up or care by parent/guardian.
- 7. **Infected wound:** Subtle pain and tenderness may be the first sign of infection. Wounds that subsequently become infected may require drainage and debridement, possibly under anesthesia. Adjust antibiotic therapy according to Gram stain and culture results.

## V. BURNS 3.15

### A. Evaluation of Pediatric Burns (Tables 4-8 and 4-9)

**NOTE:** Depending on the extent and type of burn, severity may progress over the first few days after injury; complete daily assessment necessary until burn has declared itself.

### B. Burn Mapping

Calculate total body surface area (TBSA) burned (Fig. 4-3): Based only on percentage of superficial and deep partial-thickness burns plus full-thickness burns.

### C. Emergent Management of Pediatric Burns

#### 1. Acute stabilization:

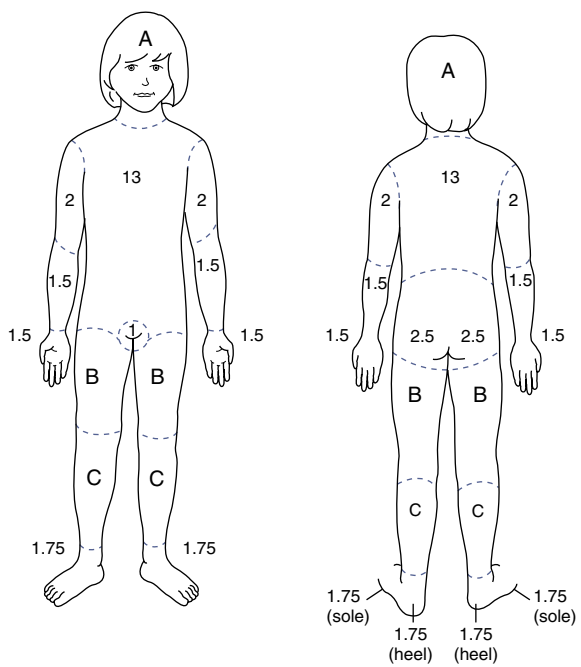
- a. Circulation:
  - (1) Start Parkland formula (Fig. 4-4) IV fluid resuscitation with normal saline for burns >15% BSA, or with any evidence of smoke inhalation.
- b. Airway with C-spine stabilization
  - (1) Assess airway for signs of inhalation injury or respiratory distress: Soot in nares, carbonaceous sputum, stridor.

TABLE 4-8  
THERMAL INJURY

Type of Burn	Description/Comment
Flame	Most common type of burn worldwide; when clothing burns, the heat exposure is prolonged, and the severity increased.
Scald/contact	Mortality for full-thickness scald burns is similar to that in flame burns when total body surface area involved is equivalent; see Fig. 4-3.
Chemical	Tissue is damaged by protein coagulation or liquefaction rather than hyperthermic activity.
Electrical	Injury is often extensive, involving skeletal muscle and other tissues in addition to the skin damage. Extent of damage may not be initially apparent. The tissues with the least resistance are most heat sensitive; bone offers the most resistance, nerve tissue the least. Cardiac arrest due to passage of current through the heart can occur.
Inhalation	Present in 30% of victims of major flame burns and increases mortality. Consider when there is evidence of fire in enclosed space. Signs include singed nares, facial burns, charred lips, carbonaceous secretions, posterior pharynx edema, hoarseness, cough, or wheezing.
Cold injury/frostbite	Freezing results in direct tissue injury. Toes, fingers, ears, and nose are commonly involved. Initial treatment includes rewarming in tepid (105°–110°F) water for 20–40 minutes. Excision of tissue should not be done until complete demarcation of nonviable tissue has occurred.

TABLE 4-9  
BURN CLASSIFICATION

Superficial	Injury to epidermis only Characterized by erythema, pain, includes sunburn or minor scalds Patients with only superficial burns do not usually require intravenous fluid replacement Not included in estimate of surface area burned Generally heals on its own without scarring in 3–5 days
Superficial partial thickness	Damages but does not destroy epidermis and dermis Characterized by intense pain, blisters, pink to cherry-red skin, moist and weepy Nails, hair, sebaceous glands, and nerves intact Can progress to deep partial- or full-thickness burn Spontaneous reepithelialization in 2–3 weeks
Deep partial thickness	Injury to epidermis and dermis Characterized by intense pain, dry and white in color Can result in disruption of nails, hair, sebaceous glands May cause scarring; skin grafting usually required
Full thickness	Injury involves all layers of skin, characterized by charred black color, ± areas dry or white Pain may be intense or absent, depending on nerve ending involvement Causes scarring; skin grafting required



	<1 yr	1 yr	5 yr	10 yr	15 yr	Adult
A Front or back of head	9.5	8.5	6.5	5.5	4.5	3.5
B Front or back of thigh	2.75	3.25	4	4.25	4.5	4.75
C Front or back of leg	2.5	2.5	2.75	3	3.25	3.5

FIGURE 4-3

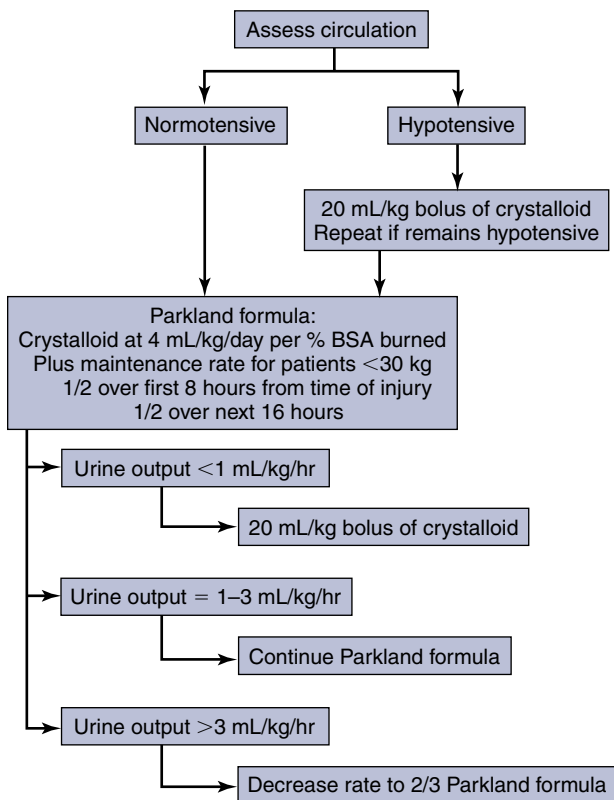
Burn assessment chart. All numbers are percentages. (From Barkin RM, Rosen P. Emergency Pediatrics: A Guide to Ambulatory Care. 6th ed. St Louis: Mosby, 2003.)

(2) Establish definitive airway early: Consider intubation for >30% TBSA burned.

**NOTE:** Avoid use of succinylcholine more than 24 hours from time of injury.

c. Breathing:

(1) Inhalation injury: Assume carbon monoxide poisoning with severe and/or closed-space burns.



- 1) Consider central venous access for burns >25% BSA.
- 2) Use the Parkland formula as a guideline to estimate fluid need. Requirements decrease by 25% to 50% after first 24 hours. Monitor weight, serum electrolytes, urine output, nasogastric losses to determine concentrations and rates.
- 3) Consider adding colloid after 18 to 24 hours (albumin, 1 g/kg/day) to maintain serum albumin >2 g/dL.
- 4) Withhold potassium generally for the first 48 hours because of a large release of potassium from damaged tissues. To manage electrolytes most effectively, monitor urine electrolytes twice weekly and replace urine losses accordingly.

**FIGURE 4-4**

Fluid management of life-threatening burns. (Modified from Nichols DG, Yaster M, Lappe DG, et al. *Golden Hour: The Handbook of Pediatric Advanced Life Support*. St Louis: Mosby, 1996:460.)

- (a) Physical examination: Symptoms may be delayed after inhalational injury occurs. Symptoms that may predict acute inhalational injury include cough, facial burns, inflamed nares, stridor, sputum production, wheezing, and altered mental status.
- (b) Management:
  - (i) Assess stability of the airway, and intubate if there are signs of airway compromise. Give aerosolized bronchodilators as needed with or without corticosteroids to decrease airway edema.  
**NOTE:** Upper airway obstruction progresses rapidly with thermal or chemical burns to the face, nares, or oropharynx.
  - (ii) Administer humidified 100% supplemental oxygen through a nonrebreather mask until carboxyhemoglobin (COHb) level <10%. Elimination half-life of COHb is dependent on  $\text{PaO}_2$  (consider hyperbaric  $\text{O}_2$  if pH <7.4 and COHb elevated). Make decisions based on  $\text{PaO}_2$  rather than pulse oximetry.
  - (iii) Check: Chest radiograph, ABGs with co-oximetry, and bedside spirometry. **NOTE:** Use co-oximetry instead of pulse oximetry to measure oxyhemoglobin.
  - (iv) Obtain 12-lead ECG to evaluate for myocardial ischemia or infarction.
  - (v) Observe for a minimum of 24 hours.

d. Exposure:

- (1) Remove clothes to stop burning process. Cool water may be used to cool patient, but then immediately wrap in dry clean blankets to prevent hypothermia.

2. **Secondary survey:** Full head-to-toe assessment.

- a. Consider associated traumatic injuries.
- b. Electrical injury can produce deep tissue damage, intravascular thrombosis, cardiac and respiratory arrest, cardiac arrhythmias, and fractures secondary to muscle contraction. Look for exit site in electrical injury.
- 3. **Assess for signs of compartment syndrome**, especially after fluid resuscitation has begun.
- 4. **GI burns:** Place gastric tube for decompression; begin prophylaxis for Curling stress ulcers with histamine-2 receptor blockers, proton-pump inhibitor, and/or antacids.
- 5. **Eye:** Ophthalmologic evaluation as necessary. Use topical ophthalmic antibiotics if abrasions are present.
- 6. **GU:** Consider Foley catheter to monitor urine output during fluid resuscitation phase.
- 7. **Pain management:** IV narcotic therapy often necessary for pain control.
- 8. **Special considerations:**
  - a. Tetanus immunoprophylaxis for patients with < three prior tetanus toxoid doses (including DTaP, DT, Td, or Tdap; patients with unknown tetanus prophylaxis history; or patients with  $\geq$  three prior tetanus toxoid doses, but last dose >5 years prior [see Chapter 16]).

- b. Chemical burns: Wash away or neutralize chemicals: brush dry chemical away and flush with copious warmed water.

#### D. Further Management of Pediatric Burns

##### 1. Inpatient management:

###### a. Indications:

- (1) Any partial-thickness burn >10% TBSA
- (2) Any full-thickness burn
- (3) Circumferential burns
- (4) Electrical, chemical, or inhalation injury
- (5) Burns of critical areas, such as face, hands, feet, perineum, or joints
- (6) Patient with underlying chronic illness, suspicion of abuse, or unsafe home environment

###### b. Outpatient management:

- (1) Indications: If burn is <10% total TBSA and does not meet previous criteria for inpatient management
- (2) Management:
  - (a) Clean with warm saline or mild soap and water. Debride open wounds and necrotic tissue.
  - (b) Apply topical antibacterial agent such as bacitracin; cover with nonadherent dressing. [See Box EC 4-A on Expert Consult.](#)
  - (c) Clean daily as mentioned previously, then change dressing. Pre-medicate with pain medication 30 minutes before each dressing change.
  - (d) Oral antibiotics not indicated.
  - (e) Follow-up within 1 week is recommended.

- c. Burn prevention: Install smoke detectors outside every bedroom and on each floor, install carbon monoxide detectors, and keep water heater temperature set <49°C (<120°F).

## VI. CHILD ABUSE

### A. Introduction

A multidisciplinary approach is warranted in cases of suspected abuse and neglect. The multidisciplinary team should include medical providers, law enforcement, social service workers, and prosecutors. Although particular populations are especially vulnerable (children with special healthcare needs and infants), children from all walks of life can be abused, so an approach to evaluating injuries should be applied uniformly.

### B. Management<sup>3,20,21</sup>

The medical professional should suspect, diagnose, treat, report, and document all cases of child abuse, neglect, or maltreatment. It is the role of the physician to report any suspected case of abuse, regardless of whether there is proof of abuse.

- 1. **Suspect:** Increase suspicion if there is inappropriate parental response, inadequate history of injury, a mechanism inconsistent with physical findings, evidence of neglect or failure to thrive, evidence of disturbed

**BOX EC 4-A****TOPICAL ANTIBACTERIAL AGENTS**

1. Bacitracin
  - Topical antibiotic
  - Poor eschar penetration
2. Silver sulfadiazine 1% cream
  - Used for full-thickness burns that cannot be immediately excised
  - Bactericidal for gram-positive and gram-negative organisms and yeast
  - Requires twice-daily dressing changes
    - Painful dressing removal
    - Better eschar penetration
  - Should not be used in those with an allergy to sulfa
3. Silver-impregnated products

emotions or expressions in a child, prior history of suspicious events, or parental substance abuse.

**NOTE:** A delay in seeking medical attention may increase suspicion of abuse, but this alone does not necessarily indicate abuse.

2. **Diagnose:** Concerning injuries. Attempt to correlate all physical findings with history; photodocument if possible (Figs. 4-5 to 4-10, color insert).
  - a. Bruises: Shape of bruises is important. Be suspicious of bruises in protected areas (chest, abdomen, back, buttocks).
    - (1) Inflicted: Located in unusual places, patterned, multiple bruises or bruises in different stages of healing, bruises that do not fit the history and developmental stage.
    - (2) Accidental: Usually located at bony surfaces such as shins, cheek, or forehead; bruises are in the same stage of healing; history fits the bruise.
  - b. Bites: Shape, size, and location are important. Intercanine distance of >3 cm is suggestive of human bites, which generally crush more than lacerate.
  - c. Burns: Signs concerning for child maltreatment include multiple burn sites, well-demarcated edges, stocking/glove distributions, absence of splash marks, symmetrically burned buttocks and/or lower legs, mirror image burns of extremities, symmetrical involvement of palms or soles, spared inguinal or other flexural creases, central sparing over buttocks or perineum, parent denial that the lesion is a burn, parent attributing the cause of the burn to a sibling, and delay in seeking medical attention.
  - d. Bleeding:
    - (1) Evaluation for retinal hemorrhages should be performed by an ophthalmologist. Retinoschisis or retinal hemorrhages that are too numerous to count, multilayered, or continue to the periphery of the retina are virtually pathognomonic for abusive head trauma.
    - (2) Duodenal hematomas are suspicious for nonaccidental blunt trauma; may lead to upper GI obstruction.
  - e. Fractures: Certain fracture types are suspicious for nonaccidental trauma ([Table 4-10](#)).
  - f. Abusive head trauma (AHT): Findings may include retinal hemorrhages, subdural hematomas, long bone or rib fractures, and CNS dysfunction (e.g., seizure, apnea, lethargy secondary to intracranial injury).
  - g. Sexual abuse:
    - (1) If abuse is suspected to have occurred within 72 hours for a child younger than age 12 or within 120 hours for a child older than 12, defer interview and GU examination at presenting facility and urgently involve a multidisciplinary team with expertise in evaluation of sexual abuse if available. Avoid collection of laboratory specimens without input from this team. Nonacute examinations falling outside of the above time windows should be deferred to a child advocacy center.
    - (2) Genital examination should be performed by trained forensic specialist, owing to anatomic variability (especially of hymen).



TABLE 4-10  
SKELETAL INJURY IN NONACCIDENTAL TRAUMA

Skeletal injury	Correlate mechanism of injury with physical finding; rule out any underlying bony pathology.
Long bones	Classic fracture is the epiphyseal/metaphyseal fracture, seen as a “bucket handle” or “corner” fracture at the end of long bones. This fracture is often secondary to jerking/shaking of a child's limb but can also be caused by natural shearing forces. Spiral fractures may be suspicious of abuse but can be seen with rotational forces (e.g., “toddler's fracture” of tibia).
Ribs	Posterior nondisplaced rib fractures are usually due to severe squeezing of the rib cage. May not be visible on plain film until callus formation.
Skull	Fractures >3 mm wide, complex fractures, bilateral fractures, and nonparietal fractures suggest forces greater than those sustained from minor household trauma.

4

(3) Normal genital examination does not rule out abuse; 95% of examinations are normal in cases of abuse.

3. **Useful studies:**

- a. Skeletal survey is suggested to evaluate suspicious bony trauma in any child; these studies are mandatory for children <2 years of age (see Chapter 25 for components).
- b. Bone scan may be indicated to identify early or difficult-to-detect fractures.
- c. Noncontrast head CT is useful for visualizing intracranial hemorrhage but unreliable for detection of skull fractures.
- d. MRI may identify lesions not detected by CT (e.g., posterior fossa injury and diffuse axonal injury).
- e. Dilated indirect ophthalmoscopy by an ophthalmologist is important for accurate detection of retinal hemorrhages in suspected AHT.

4. **Treat:** Medical stabilization is primary goal. Prevention of further injuries is the long-term goal.

5. **Report:** All healthcare providers are required by law to report suspected child maltreatment to the local police and/or child welfare agency. Suspicion supported by objective evidence is criterion for reporting and should first be discussed with not only the entire medical team but also the family. The professional who makes such reports is immune from any civil or criminal liability.

6. **Document:** Write legibly, carefully documenting the following: reported and suspected history and mechanisms of injury, any history given by the victim in his or her own words (use quotation marks), information provided by other providers or services, and physical examination findings, including drawings of injuries and details of dimensions, color, shape, and texture. Always consider early use of police crime laboratory photography to document injuries.

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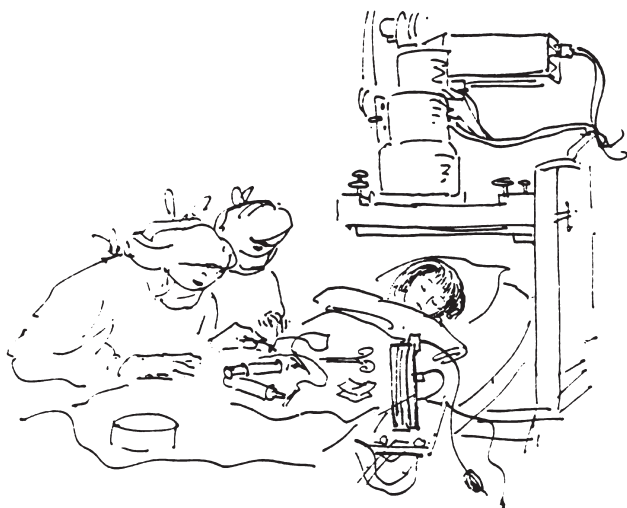
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## PART II

# DIAGNOSTIC AND THERAPEUTIC INFORMATION



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# Chapter 5

## Adolescent Medicine

Natalie Spicyn, MD, MHS



See additional content on Expert Consult

### I. WEBSITES

#### A. Websites for Clinicians

American Academy of Pediatrics (AAP) section on adolescent health:

<http://www.aap.org/sections/adolescenthealth>

Adolescent development: <http://www.aacap.org>

Sexual and reproductive health, including minor consent laws: <http://www.guttmacher.org/sections/adolescents.php>

#### B. Websites for Patients

Sexual health: <http://www.ashastd.org>

Drug abuse: <http://teens.drugabuse.gov>

### II. INTRODUCTION TO ADOLESCENT HEALTH

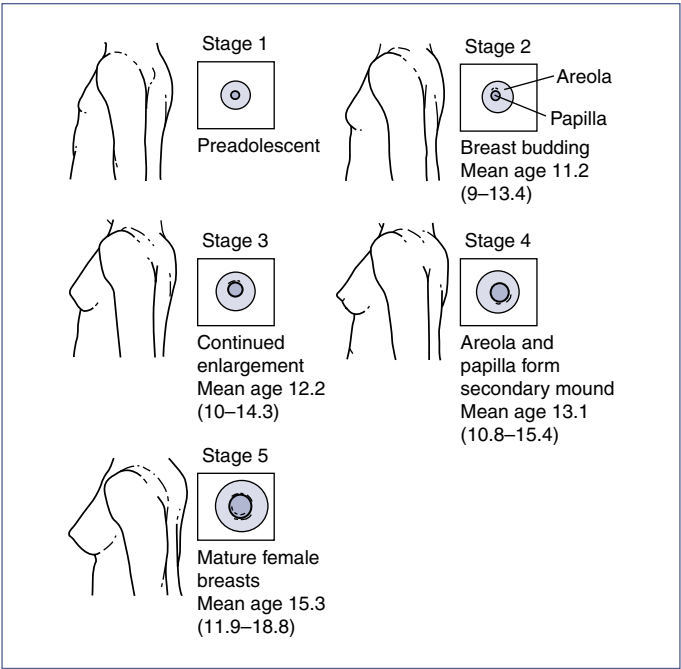
#### A. Pubertal Development<sup>1-5</sup>

1. **Pubic hair** (for males and females); (Table 5-1)
2. **Female breast development** (Fig. 5-1)
3. **Male genital development** (Table 5-2). Also see Table 10-16 for testicular volumes
4. **Gynecomastia in males**
  - a. Generally occurs in middle–late stages of puberty.
  - b. Etiology: Breast growth stimulated by estradiol.
  - c. Prevalence: Occurs in 50% of boys (50% unilateral, 50% bilateral).
  - d. Clinical course: Regression usually occurs over 2-year period.
  - e. Physical examination: With patient supine, palpate breast looking for glandular or fibroglandular breast tissue beneath nipple and areola, comparing to the lateral breast tissue to distinguish true gynecomastia from adiposity, pseudogynecomastia, or a pathologic etiology. A testicular examination should also be performed.
  - f. Treatment: Often no treatment is necessary. Severe or nonregressing cases may warrant surgical referral.
5. **Precocious puberty:** Onset of secondary sexual characteristics before age 8 in girls and age 9 in boys.
6. **Delayed puberty:** Lack of secondary sexual development by age 14 (see Figure 10-5 for more information on the approach to a child with delayed puberty).

#### B. Psychosocial Development (Table EC 5-A available on Expert Consult).

**TABLE 5-1**  
**PUBIC HAIR TANNER STAGING**

Tanner Stage	Appearance
1	No hair
2	Sparse, downy hair at base of symphysis pubis
3	Sparse, coarse hair across symphysis pubis
4	Adult hair quality, fills in pubic triangle, no spread to thighs
5	Adult quality and distribution including spread to medial thighs



**FIGURE 5-1**

Tanner stages of breast development in females. (Modified from Johnson TR, Moore WM. Children Are Different: Developmental Physiology. 2nd ed. Columbus, Ohio, Ross Laboratories, 1978. Mean age and range [2 standard deviations around mean] from Joffe A. Introduction to adolescent medicine. In McMillan JA, DeAngelis CD, Feigin RD, et al, eds. Oski's Pediatrics: Principles and Practice. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2006:549-550.)



TABLE EC 5-A

## PSYCHOSOCIAL DEVELOPMENT OF ADOLESCENTS

Task	Early Adolescence (10–13 yr)	Middle Adolescence (14–16 yr)	Late Adolescence (>17 yr)
Independence	Less interest in parental activities Wide mood swings	Peak of parental conflicts	Reacceptance of parental advice and values
Body image	Preoccupation with self and pubertal changes Uncertainty about appearance	General acceptance of body Concern over making body more attractive	Acceptance of pubertal changes
Peers	Intense relationships with same-sex friend	Peak of peer involvement Conformity with peer values Increased sexual activity and experimentation	Peer group less important More time spent in sharing intimate relationships
Identity	Increased cognition Increased fantasy world Idealistic vocational goals Increased need for privacy Lack of impulse control	Increased scope of feelings Increased intellectual ability Feeling of omnipotence Risk-taking behavior	Practical, realistic vocational goals Refinement of moral, religious, and sexual values Ability to compromise and to set limits

From Joffe A. Introduction to adolescent medicine. In McMillan JA, DeAngelis CD, Feigin RD, et al, eds. *Oski's Pediatrics: Principles and Practice*. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2006:.

TABLE 5-2

## GENITAL DEVELOPMENT (MALE)

Stage	Comment ( $\pm 2$ Standard Deviations Around Mean Age)
1	Prepubertal
2	Enlargement of scrotum and testes; skin of scrotum reddens and changes in texture; little or no enlargement of penis; mean age 11.4 yr (9.5–13.8 yr)
3	Enlargement of penis, first mainly in length; further growth of testes and scrotum; mean age 12.9 yr (10.8–14.9 yr)
4	Increased size of penis with growth in breadth and development of glans; further enlargement of testes and scrotum and increased darkening of scrotal skin; mean age 13.8 yr (11.7–15.8 yr)
5	Genitalia adult in size and shape; mean age 14.9 yr (13–17.3 yr)

Data from Joffe A. Introduction to adolescent medicine. In McMillan JA, DeAngelis CD, Feigin RD, et al, eds. *Oski's Pediatrics: Principles and Practice*. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2006:546–557.

C. Psychosocial and Medicosocial History<sup>6,7,27</sup>

HEADSSS<sup>3,4,6</sup>: Brief instrument that screens for psychosocial factors that impact adolescent mental and physical health (Box 5-1)

## BOX 5-1

## HEADSSS ASSESSMENT

- (H)OME:** Household composition, family dynamics and relationships, living and sleeping arrangements, recent changes, any periods of homelessness, running away from home
- (E)DUCATION/EMPLOYMENT/EATING:** School performance, attendance, suspensions; attitude toward school; favorite, most difficult, best subjects; special educational needs; goals for the future; afterschool job or other work history (see Section III.C, Review of Systems, for eating/nutrition questions)
- (A)CTIVITIES:** Friendships with same or opposite sex, ages of friends, best friend, dating, recreational activities, physical activity, sports participation, hobbies and interests
- (D)RUGS:** Personal use of tobacco, alcohol, illicit drugs, anabolic steroids; peer substance use; family substance use and attitudes; if personal use, determine frequency, quantity, binge, injury with use; consider use of **CRAFFT** questionnaires (Box 5-2)
- (S)EXUALITY:** See Box EC 5-A for the "Five Ps" of the sexual history; additional helpful information includes age at first sex, number of lifetime and current partners, ages of partners, recent change in partners; knowledge of emergency contraception and sexually transmitted infection/human immunodeficiency virus (STI/HIV) prevention; prior testing for STI/HIV, prior pregnancies, abortions; ever fathered a child; history of nonconsensual intimate physical contact or sex
- (S)UICIDE/DEPRESSION:** Feelings about self, both positive and negative; history of depression or other mental health problems; sleep problems (difficulty getting to sleep, early waking); changes in appetite or weight; anhedonia; irritability; anxiety; current or prior suicidal thoughts or attempts; other self-harming or injurious behavior
- (S)AFETY:** Feeling unsafe at home, at school, or in the community; bullying; guns in the home; weapon carrying, what kinds of weapons; fighting; arrests; gang membership

## BOX EC 5-A

**OBTAINING THE SEXUAL HISTORY: THE FIVE Ps****1. Partners**

- "Do you have sex with men, women, or both?"
- "In the past 2 months, how many partners have you had sex with?"
- "In the past 12 months, how many partners have you had sex with?"
- "Is it possible that any of your sex partners in the past 12 months had sex with someone else while they were still in a sexual relationship with you?"

**2. Prevention of Pregnancy**

- "What are you doing to prevent pregnancy?"

**3. Protection from STIs**

- "What do you do to protect yourself from STIs and HIV?"

**4. Practices**

- "To understand your risk for STIs, I need to understand the kind of sex you have had recently."
- "Have you had vaginal sex, meaning 'penis in vagina sex'?" If yes, "Do you use condoms: never, sometimes, or always?"
- "Have you had anal sex, meaning 'penis in rectum/anus sex'?" If yes, "Do you use condoms: never, sometimes, or always?"
- "Have you had oral sex, meaning 'mouth on penis/vagina sex'?"  
For condom answers:
  - If "never": "Why don't you use condoms?"
  - If "sometimes": "In what situations, or with whom, do you not use condoms?"

**5. Past History of STIs**

- "Have you ever had an STI?"
- "Have any of your partners had an STI?"  
Additional questions to identify HIV and viral hepatitis risk include:
  - "Have you or any of your partners ever injected drugs?"
  - "Have any of your partners exchanged money or drugs for sex?"
  - "Is there anything else about your sexual practices I need to know about?"

HIV, Human immunodeficiency virus; STI, sexually transmitted infection.

Modified from the Centers for Disease Control and Prevention (CDC) *Sexually Transmitted Diseases Treatment Guidelines 2010, Clinical Prevention Guidance*. Available at <http://www.cdc.gov/std/treatment/2010/clinical.htm#box1>.

**BOX 5-2****CRAFT QUESTIONNAIRE<sup>27</sup>**

**C**—Have you ever ridden in a **CAR** driven by someone (or yourself) who was “high” or had been using alcohol or drugs?

**R**—Do you ever use alcohol or drugs to **RELAX**, feel better about yourself, or fit in?

**A**—Do you ever use alcohol/drugs while you are **ALONE**?

**F**—Do your family or **FRIENDS** ever tell you that you should cut down on your drinking or drug use?

**F**—Do you ever **FORGET** things you did while using alcohol or drugs?

**T**—Have you gotten into **TROUBLE** while you were using alcohol or drugs?

**NOTE:** Answering yes to two or more questions is a positive screen.

**III. ADOLESCENT HEALTH MAINTENANCE**

Bright Futures Guidelines for Health Supervision of Adolescents<sup>8</sup>

(Box EC 5-B on Expert Consult)

**A. Confidentiality**

Adolescents are concerned about the confidentiality of their interactions with healthcare providers. Laws governing minors' ability to consent to health care vary by state and type of service. More information can be found at the Guttmacher Institute's website ([http://www.guttmacher.org/statecenter/spibs/spib\\_OMCL.pdf](http://www.guttmacher.org/statecenter/spibs/spib_OMCL.pdf)).

**B. Chief Complaint**

Hidden agenda: Adolescents may state a chief complaint that is not always the real concern for the visit. Upon initiating a visit, reviewing the reason for the visit ("What brings you in today?" "Is there anything else?") can reveal the actual reason.

**C. Review of Systems (Areas of Emphasis with an Adolescent)**

1. **Nutrition:** Dietary habits, including skipped meals, special diets, purging methods, recent weight gain or loss
2. **Skin:** Acne, moles, rashes, warts
3. **Genitourinary:** Dysuria, urgency, frequency, discharge, bleeding
4. **Menstrual:** Menarche, frequency, duration, pain, menometrorrhagia

**D. Family History<sup>3,4</sup>**

Including psychiatric disorders, suicide, alcoholism or substance abuse, and chronic medical conditions or familial risk factors (hypertension, diabetes, cholesterol, blood clot, heart attack, stroke, cancer, asthma, tuberculosis, HIV).

**E. Physical Examination (Most Pertinent Aspects)<sup>3,4,8-10</sup>**

Whenever possible, examine patient in a gown to ensure a complete and thorough examination.

1. **Height, weight (calculate body mass index [BMI]), and blood pressure with percentiles.**
2. **Dentition and gums** (smokeless tobacco use, enamel erosion from induced vomiting).

## BOX EC 5-B

## BRIGHT FUTURES GUIDELINES FOR HEALTH SUPERVISION OF ADOLESCENTS

Health guidance for teens and parents	Physical growth and development (physical and oral health, body image, healthy eating, physical activity) Violence and injury prevention (safety belt and helmet use, substance abuse and riding in a vehicle, guns, interpersonal violence [fights], bullying) Social and academic competence (connectedness with family, peers, and community; interpersonal relationships; school performance) Emotional well-being (coping, mood regulation and mental health, sexuality) Risk reduction (tobacco, alcohol and other drugs, pregnancy, STIs)
Screening	Dyslipidemia, <sup>†</sup> pregnancy and STI if sexually active, <sup>†</sup> alcohol or drug use, <sup>†</sup> tuberculosis, <sup>†</sup> anemia, <sup>†</sup> hearing, <sup>†</sup> and vision <sup>*</sup>
Tests	Tuberculin skin test, Pap smear at age 21, HIV status, <sup>‡</sup> screen for chlamydia and gonorrhea (use tests appropriate to patient population and clinical setting), syphilis blood test, lipid screen, hemoglobin or hematocrit, Snellen test, audiometry, alcohol and drug screening tools

5

\*Universal screening once in early adolescence.

<sup>†</sup>Selective screening if patient screens positive on risk screening questions.

<sup>‡</sup>The Centers for Disease Control and Prevention (CDC) recently recommended universal voluntary HIV screening for all sexually active persons beginning at age 13. The health care professional's attention is drawn to the voluntary nature of screening and that the CDC allows an opt out in communities where the HIV rate is <0.1%.

HIV, Human immunodeficiency virus; STI, sexually transmitted infection.

From American Academy of Pediatrics. *Bright Futures Guidelines for Health Supervision of Infants, Children, and Adolescents*. 3rd ed. Elk Grove, Village, IL: AAP, 2008. Available at <http://brightfutures.aap.org>.

3. **Skin:** Acne (type and distribution of lesions), atypical nevi, acanthosis nigricans, scars, piercings, tattoos
4. **Thyroid**
5. **Spine:** Routine screening for idiopathic scoliosis is not recommended owing to unfavorable balance of risks and benefits, but clinicians should be prepared to evaluate scoliosis if incidentally discovered or the patient or parent expresses concern.  
[More information about assessment and treatment of scoliosis is available on Expert Consult.](#)
6. **Breasts:** Sexual maturity rating for females (see [Fig. 5-1](#)), masses (females); gynecomastia (males)
7. **Genitalia:** For both male and female genital examinations, talk patients through examination, commenting on normal findings. Touch a nongenital part of body first, examine painful areas last. Avoid lengthy discussions while patients are undressed and in a compromising position. Consider use of a chaperone.
  - a. Male:
    - (1) Visual inspection for sexual maturity rating for hair ([Table 5-2](#), see [Table 10-16](#)) and signs of STI (e.g., warts, lice, ulcers, discharge)
    - (2) Genital examination for sexual maturity rating for testicles (see [Table 10-16](#)) and identification of masses, hydrocele, varicocele, hernias
  - b. Female:
    - (1) External examination: Visual inspection of perineum (warts, ulcers, rashes, pubic lice, trauma, discharge) and sexual maturity rating for hair (Tanner stage, see [Table 5-1](#)).
    - (2) Internal examination (pelvic examination): Indications include vaginal discharge (assess cervix for mucopurulent discharge, friability, large ectropion, foreign body); lower abdominal or pelvic pain; urinary symptoms in a sexually active female; menstrual disorders (amenorrhea, abnormal vaginal bleeding, or dysmenorrhea refractory to medical therapy); consideration of intrauterine device or diaphragm (not necessary before prescription of other methods of contraception); and suspected or reported sexual abuse or rape (refer to a specialized center if not trained and equipped to appropriately document evidence of trauma and collect forensic specimens).
  - c. Anal inspection for patients engaging in anal sex.

## F. Screening Laboratory Tests and Procedures<sup>8,11-16</sup>

1. **A dearth of research and evidence for screening examinations for adolescence** has led to variability in guidelines for topics such as screening for dyslipidemia, iron-deficiency anemia, diabetes, and tuberculosis. Updated guidelines issued by various organizations

**Scoliosis**<sup>26,28</sup>:

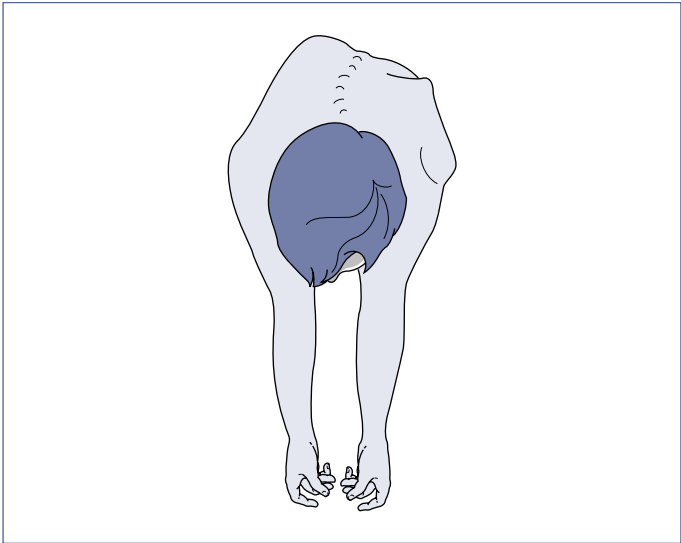
## a. Assessment

- (1) *Adams forward bend test*. Ask patient to bend forward at the hips, with knees straight and arms hanging forward. Spine is inspected from behind for symmetry. Emphasizes any asymmetry of the paraspinous muscles and rib cage (Fig. EC 5-A).
- (2) *Scoliometer*. Place midline over spot of maximum rotation during Adams forward bend test. Threshold of 5 to 7 degrees of rotation roughly correlates to 20-degree Cobb angle and is often used as cutoff for orthopedic referral.
- (3) Radiographic determination of Cobb angle (Fig. EC 5-B). If there is clinical suspicion of significant scoliosis on screening, obtain erect thoracoabdominal spinal view.
- (4) Bone scan with or without magnetic resonance imaging (MRI): If pain is worse at night, progressive, well localized, or otherwise suspicious, obtain bone scan or MRI to look for tumor, infection, or fracture.
- (5) MRI: Obtain if patient is younger than 10 years or if *opposite* curves are present (i.e., left-sided thoracic and right-sided lumbar)

## b. Treatment

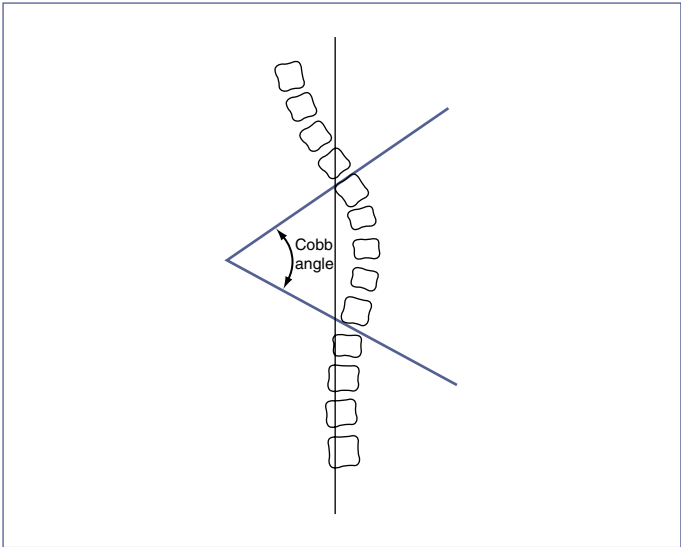
Treatment plan determined according to Cobb angle and skeletal maturity (assessed by grading ossification of iliac crest). Skeletal maturity can be estimated in females; typically reached 18 months after menarche.

- (1) Skeletally immature:
  - (a) <10 degrees: Obtain single follow-up radiograph in 4–6 months to ensure there has been no significant progression of scoliosis.
  - (b) 10–20 degrees: Obtain follow-up radiographs every 4–6 months while still growing
  - (c) 20–40 degrees: Bracing required
  - (d) >40 degrees: Surgical correction necessary
- (2) Skeletally mature:
  - (a) <40 degrees: No further evaluation or intervention indicated
  - (b) >40 degrees: Surgical correction required
- (3) Orthopedic referral: Indicated if patient is skeletally immature with a curve > 20 degrees, skeletally mature with a curve > 40 degrees, or in the presence of suspicious pain or neurologic symptoms



**FIGURE EC 5-A**

Forward bending test. This emphasizes any asymmetry of the paraspinous muscles and rib cage.



**FIGURE EC 5-B**

Cobb angle. This is measured using the superior and inferior end plates of the most tilted vertebrae at the end of each curve.



may be accessed at the listed sites; recommendations that follow are largely based on CDC guidelines:

- a. Bright Futures<sup>8</sup>: <http://brightfutures.aap.org>
  - b. CDC: <http://www.cdc.gov/HealthyYouth/index.htm>
  - c. U.S. Preventive Services Task Force (USPSTF): <http://www.uspreventiveservicestaskforce.org/tfchildcat.htm>
2. **Adolescents may legally consent to medical care for STIs without parental notification** in all 50 states and Washington, D.C., but providers should be aware of barriers to confidentiality related to medical billing and explanation of benefits by insurance companies.
- CDC STI screening guidelines for sexually active adolescents are as follows<sup>17</sup>:
- a. HIV: Routine screening recommended starting at age 13, with subsequent tests at least annually for all persons at high risk.<sup>13</sup> Rescreening for both HIV and syphilis 3–4 months after a documented STI. Remember that screening (antibody) testing will not pick up acute infection, so if concerned about the clinical syndrome of acute HIV infection, ribonucleic acid (RNA) testing should be ordered.
  - b. Syphilis: Routine screening recommended annually for persons at risk.
  - c. Chlamydia and gonorrhea:
    - (1) *Chlamydia trachomatis* (CT): Routine screening in sexually active persons < age 25. For males, screening especially recommended in high prevalence communities and/or settings (e.g., STI clinics, adolescent clinics, correctional facilities).
    - (2) *Neisseria gonorrhoeae* (GC) testing recommended for all sexually active female adolescents. Among young men who have sex with men (YMSM), at least annual testing is also recommended, with attention to site of collection (urine for insertive partner, rectal swab for receptive partner, pharyngeal swab for receptive partner in oral intercourse).
    - (3) Female: Self- or provider-collected vaginal nucleic acid amplification test (NAAT) is preferred method to screen for CT/GC; self-collected specimens may have higher patient acceptability. Vaginal swabs are as sensitive and specific as cervical samples; urine samples are less so.
    - (4) Male: Urine NAAT is preferred method to screen for CT/GC. Sexually active adolescent males are considered. YMSM specifically for GC.
    - (5) Patients who test positive for chlamydia should be rescreened 3–4 months after treatment; rates of reinfection are high.<sup>14</sup>
    - (6) Patients with gonorrhea: Consider test of cure 3–4 weeks later if patients did not receive CDC-recommended or alternative antibiotic regimens.
  - d. Other STIs:
    - (1) Routine screening of asymptomatic adolescents not recommended for other STIs (e.g., trichomoniasis, herpes simplex virus [HSV], hepatitis A and B viruses [HAV, HBV], human papillomavirus [HPV]).
    - (2) Refer to CDC guidelines for specific additional recommendations for STI screening among YMSM who might require more thorough evaluation.

### 3. Cervical cancer cytologic analysis (Papanicolaou [Pap] smear)<sup>11,12</sup>:

- a. *Immunocompetent*: Regardless of age of sexual debut, cervical cancer screening with Pap smear should not begin until a woman is 21 years old. Subsequent tests should be done every 3 years. Cytologic evaluation only should be used; HPV testing is indicated until age 30.
- b. *HIV+ or immunosuppressed (e.g., organ transplant recipient, systemic lupus erythematosus patient, poorly controlled diabetic)*: Every 6 months in first year after HIV diagnosis or after sexual debut if immunosuppressed; thereafter, annually.
- c. In immunocompetent adolescents, risk of adverse pregnancy outcomes outweighs benefits of screening and treatment, given the low rate of cervical cancer and high rate of resolution of HPV infections. However, immunocompetent adolescents who have had abnormal cytologic study results may be treated according to [Table EC 5-B \(available on Expert Consult\)](#). Immunosuppressed adolescents with abnormal cytologic results should be referred for further management.

### G. Immunizations

Refer to Chapter 16 for dosing, route, formulation, and schedules.

## IV. PREPARTICIPATION PHYSICAL EVALUATION (PPE)<sup>13,14</sup>

PPE is an opportunity to screen for risks related to participation in sports but is also an opportunity to deliver adolescent clinical preventive services, because this may be a young person's only visit during adolescence.

### A. Medical History

Includes information about chronic conditions/medications (including performance-enhancing agents), hospitalizations/surgeries, use of protective equipment during sports participation, allergies (especially those associated with anaphylaxis, respiratory compromise, or exercise-induced), and immunizations (HBV; measles, mumps, rubella [MMR]; tetanus; varicella).

**NOTE:** See Chapter 7, Table 7-14, and Table EC 7-D for further information about PPE screening and exercise restrictions with cardiac disease.

### B. Review of Systems and Physical Examination

*(Physical examination items in italics.)*

1. **Height and weight**
2. **Vision:** Visual problems, corrective lenses, visual acuity, pupil equality
3. **Cardiac:** History of congenital heart disease; syncope, dizziness, or chest pain during exercise; history of high blood pressure or heart murmurs; family history of heart disease; history of disqualification or limited participation in sports because of a cardiac problem; *blood pressure, heart rate and rhythm, pulses (including radial/femoral lag), auscultation of heart sounds, murmurs—both standing and supine*
4. **Respiratory:** Asthma, coughing, wheezing, or dyspnea during exercise
5. **Abdomen:** *Organomegaly* and single kidney are contraindications for contact sports

TABLE EC 5-B

**SUMMARY OF TREATMENT RECOMMENDATIONS FOR CYTOLOGIC AND HISTOLOGIC ABNORMALITIES IN IMMUNOCOMPETENT ADOLESCENTS**

Diagnosis	ACOG Recommendations for Immunocompetent Adolescents
ASC-US, LSIL, CIN 1	Repeat cytology at 12-month intervals for 2 years; if negative, reinitiate screening at age 21
ASC-H	Colposcopy; if no CIN 2-3 identified, cytology at 6-month intervals until 2 consecutive normal Pap test results
HSIL	Colposcopy; if no CIN 2-3 on biopsy, colposcopy and cytology at 6-month intervals
ACG	Colposcopy, endocervical assessment, possible endometrial evaluation
CIN 2	Cytology and colposcopy at 6-month intervals for up to 24 months; observation preferred to treatment
CIN 3	Therapy; particular intervention per recommendation of gynecologist (cryotherapy vs. laser therapy vs. LEEP)

ACOG, American College of Obstetricians and Gynecologists; AGC, atypical glandular cells; ASC-US, atypical squamous cells—undetermined significance; ASC-H, atypical squamous cells—cannot exclude HSIL; CIN, cervical intraepithelial neoplasia; HSIL, high-grade squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesion; LEEP, loop electrosurgical excision procedure; Pap, papanicolaou.

From American College of Obstetricians and Gynecologists. *Cervical Cancer in Adolescents: Screening, Evaluation, and Management*. Committee Opinion No. 463. *Obstet Gynecol*. 2010;116:469-472.

6. **Genitourinary:** Age at menarche, last menstrual period, regularity of menstrual periods, number of periods in the last year, longest interval between periods, dysmenorrhea; *palpation of abdomen, palpation of testicles, examination of inguinal canals*
7. **Orthopedic:** Previous injuries that have limited sports participation or required medical intervention; screening orthopedic examination (Fig. EC 5-C available on Expert Consult). Consider checking vitamin D levels if history of a fracture with minor trauma.
8. **Neurology:** History of significant head injury/concussion, numbness or tingling of extremities, severe headaches, seizure disorder (although not an absolute contraindication to contact sports if well controlled, seizure within past 6 months should raise concern prior to clearance, particularly for those engaged in water sports)
9. **Skin:** Rashes; *evidence of contagious infections (e.g., varicella or impetigo)*
10. **Psychosocial:** Weight control and body image, stressors at home or in school, use or abuse of drugs and alcohol; *attention to signs of eating disorders, including oral ulcerations, eroded tooth enamel, edema, lanugo hair, calluses or ulcerations on knuckles*

## V. SEXUAL HEALTH 120-25

### A. Sexual Orientation

Adolescents may explore a variety of sexual activities (penile-vaginal, anal, or oral intercourse) but not equate behaviors with sexual identity or orientation (e.g., heterosexual, homosexual, bisexual). Conversely, adolescents may self-identify with a particular sexual orientation but not be sexually active.

### B. Gender Identity

Refers to an individual's self-awareness as male or female:

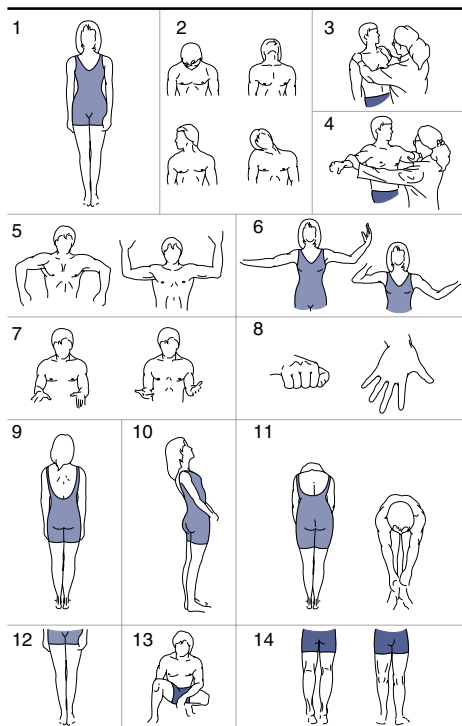
1. **Transgender:** An individual whose gender identity (internal sense) or gender expression (behavior, etc.) differs from the biological sex assigned at birth
2. **Transvestite:** An individual who derives pleasure from dressing in clothing of the opposite sex
3. **Gender identity is unrelated to sexual orientation;** transgender or transvestite individuals may feel themselves to be heterosexual, homosexual, or bisexual

### C. Contraception

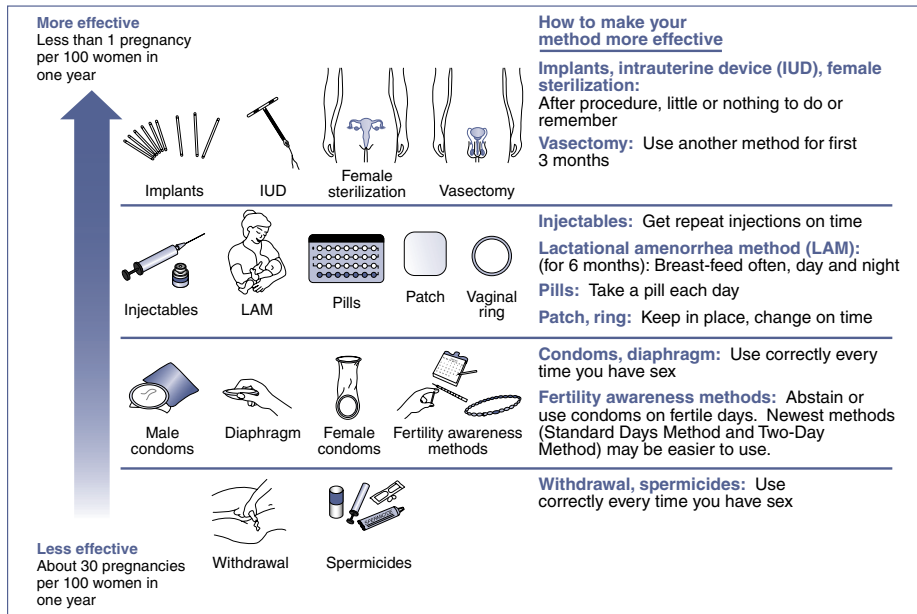
#### 1. Special considerations in adolescents

- a. Barriers may include confidentiality concerns, fear of the pelvic examination, and fear of side effects (e.g., weight gain, bleeding, etc.).
- b. Adherence and continuation rates in adolescents are superior with long-acting reversible contraception (LARC) methods such as the intrauterine device and etonogestrel implant.
- c. Counseling should include discussion of need for barrier method to prevent STIs, as well as tips for increasing adherence.

#### 2. Methods of contraception (Fig. 5-2)

**FIGURE EC 5-C**

Screening orthopedic examination. The general musculoskeletal screening examination consists of: 1, inspection with athlete standing, facing examiner (symmetry of trunk, upper extremities); 2, forward flexion, extension, rotation, lateral flexion of neck (cervical spine range of motion [ROM]); 3, resisted shoulder shrug (trapezius strength); 4, resisted shoulder abduction (deltoid strength); 5, internal and external rotation of shoulder (glenohumeral joint ROM); 6, extension and flexion of elbow (elbow ROM); 7, pronation and supination of elbow (elbow, wrist ROM); 8, clenching of fist, then spreading of fingers (hand, fingers ROM); 9, inspection with athlete facing away from examiner (symmetry of trunk, upper extremities); 10, back extension, knees straight (spondylolysis, spondylolisthesis); 11, back flexion with knees straight, facing toward and away from examiner (thoracic and lumbosacral spine ROM, spine curvature, hamstring flexibility); 12, inspection of lower extremities, contraction of quadriceps muscles (alignment symmetry); 13, "duck walk" four steps (motion of hips, knees, ankles; strength; balance); 14, standing on toes, then on heels (calf symmetry, strength, balance). (Based on figures created by Rebekah Dodson and Terry Boles in *Preparticipation Physical Examination*, 3rd ed. McGraw Hill, 2005.)

**FIGURE 5-2**

Comparing effectiveness of family planning methods. (From World Health Organization Department of Reproductive Health and Research [WHO/RHR] and Johns Hopkins Bloomberg School of Public Health/Center for Communication Programs [CCP], Knowledge for Health Project. Family Planning: A Global Handbook for Providers (2011 Update). Baltimore, Geneva: CCP and WHO, 2011.)

### 3. Contraception selection and initiation:

#### a. Selecting a contraceptive method<sup>22</sup>

Please refer to the CDC's Medical Eligibility Criteria (<http://www.cdc.gov/mmwr/pdf/rr/rr59e0528.pdf>) for any relative or absolute contraindications for each hormonal contraceptive method based on an individual's medical comorbidities and the CDC's Selected Practice Recommendations for minimum requirements to start each method.

- (1) To appropriately start a hormonal method, the basic medical history should include assessment of clotting risk, blood pressure, pregnancy status, and any other pertinent medical comorbidities.
- (2) Related to clotting symptoms for a person on a combined method, a mnemonic to remember the more serious complications of combined hormonal contraception is ACHES<sup>23</sup>:
  - (a) **A**bdominal pain (pelvic vein or mesenteric vein thrombosis, pancreatitis)
  - (b) **C**hest pain (pulmonary embolism)
  - (c) **H**eadaches (thrombotic or hemorrhagic stroke, retinal vein thrombosis)
  - (d) **E**ye symptoms (thrombotic or hemorrhagic stroke, retinal vein thrombosis)
  - (e) **S**evere leg pain (thrombophlebitis of the lower extremities)
- (3) To support adherence and continuation, use a patient-centered approach, review method effectiveness, and provide anticipatory guidance regarding side effects of each method when assisting an adolescent in selecting a new contraceptive method.

#### b. Quick start<sup>25</sup>

Defined as starting a method of contraception on the day of the visit (not waiting until a new menstrual cycle begins) (Fig. 5-3)

Principles of quick-start contraception regimens:

- (1) Initiate method immediately to decrease confusion and prevent patient's failure to properly initiate contraception during subsequent menstrual cycle.
- (2) Rule out pregnancy; advise that a pregnancy test at quick-start initiation is not conclusive, but hormones will not affect pregnancy.
- (3) Provide emergency contraception (EC) if indicated (see Section V.C.5).
- (4) Counsel youth to use condoms for 1 week and obtain a follow-up pregnancy test in 4 weeks if the method was initiated after day 6 of the menstrual cycle.

### 4. Patient use instructions for various contraceptive methods<sup>22-24</sup>

#### a. Combined hormonal oral contraceptive pills (OCPs):

- (1) Take one pill at the same time each day (within a 4-hour window).
- (2) The first pill should be taken either on the day of the visit (quick start) or between the first and seventh day after the start of the menstrual period (most commonly Sunday).
- (3) Some pill packs have 28 pills, others have 21 pills. When the 28-day pack is empty, immediately start taking pills from a new

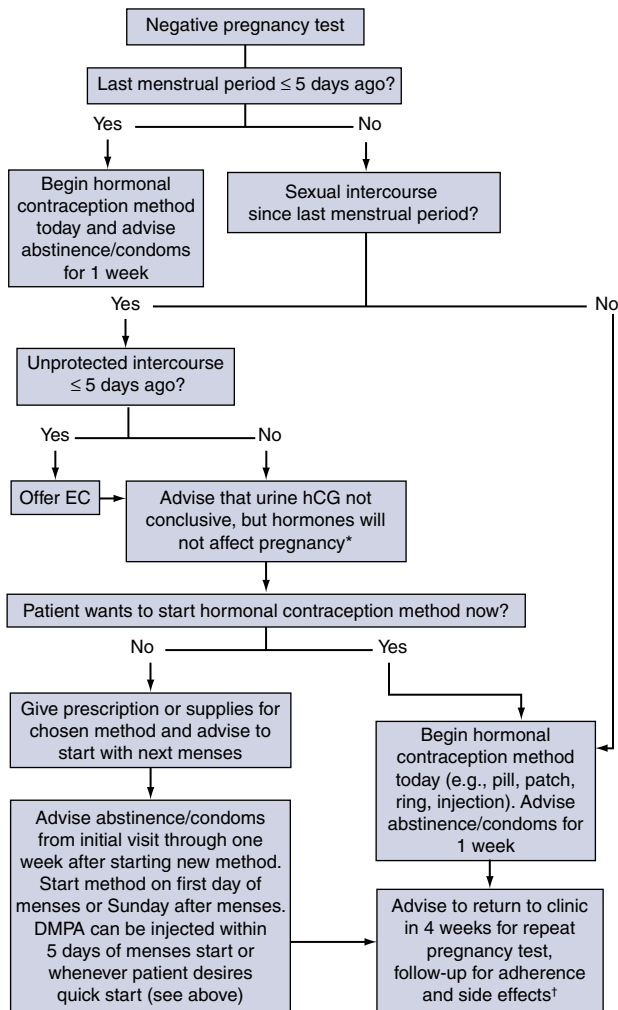


FIGURE 5-3

Algorithm for quick-start initiation of contraception. EC, Emergency contraception; hCG, human chorionic gonadotropin. \*Pregnancy tests may take 2–3 weeks after sex to be accurate. †Consider pregnancy test at second depot medroxyprogesterone acetate (DMPA [Depo-Provera]) injection if quick-start regimen was used and patient failed 4-week follow-up visit. (Modified from Zieman M, Hatcher RA, Cwiak C, et al. *A Pocket Guide to Managing Contraception*. Tiger, Georgia: Bridging the Gap Foundation, 2010:142.)



pack. When the 21-day pack is empty, wait 1 week (7 days), then begin taking pills from a new pack.

- (4) If you vomit within 30 minutes of taking a pill, take another pill or use a backup method if you have sex during the next 7 days.
- (5) If you forget to take a pill, take it as soon as you remember, even if it means taking two pills in 1 day.
- (6) If you forget to take two or more pills, take two pills every day until you are back on schedule. Use a backup method (e.g., condoms) or do not have sex for 7 days.
- (7) If you miss two or more menstrual periods, come to the clinic for a pregnancy test.
- (8) If you feel nauseous on the pills, consider changing the time of day you take them.

b. Transdermal (patch) contraceptive:

- (1) Apply within 1–5 days after the onset of menses (first day is preferred) or quickstart. Place on upper arm or upper back but not over chest or breast area.
- (2) Replace weekly for 3 weeks.
- (3) Allow 1 week without patch for menses, then restart cycle.
- (4) Rotate location of patch to avoid skin irritation.
- (5) If patch falls off, put on new patch as soon as possible and use a backup method of contraception.

c. Vaginal ring:

- (1) Place ring in vagina for 3 weeks.
- (2) Remove ring for 1 week for withdrawal bleeding.
- (3) Place new ring in vagina for 3 weeks.
- (4) If ring is expelled, rinse with water and reinsert; backup contraception is needed if ring is out for > 3 hours.

d. Depot medroxyprogesterone acetate (DMPA [Depo-Provera]) injection:

- (1) Initial injection within first 5 days after onset of menses (or quick start; see [Fig. 5-3](#))
- (2) Reinjection every 11–13 weeks (depending on whether injection is intramuscular [IM] or subcutaneous [SQ])
- (3) If bleeding is bothersome, consider asking your doctor about a 7–10 day course of conjugated estrogen.

5. **Emergency contraception (EC)**<sup>21,22</sup>

a. Methods:

- (1) Progestin only: Levonorgestrel 1.5 mg orally (PO) once (brand name "Plan B One Step" or "Next Choice" with older formulation; "Plan B" consisting of two 0.75-mg tablets that patients should be instructed to take together, regardless of packet instructions). Most efficacious within 72 hours of coitus but effective through 120 hours; ulipristal has superior efficacy in the 72–120 hour window.
- (2) Selective progesterone receptor modulator: Ulipristal 30 mg PO once.
- (3) Combined hormonal: Known as the "Yuzpe method," involves counseling patients to take two doses of OCPs, with each dose containing

at least 100 mcg of ethinyl estradiol and at least 500 mcg of levonorgestrel (either 8 total tablets: 4 at a time, 12 hours apart, or for more precise instructions for a particular combination pill; refer to [www.ec.princeton.edu](http://www.ec.princeton.edu)). Consider prescribing an antiemetic, such as metoclopramide or meclizine, for use 1 hour before first dose.

- (4) Copper intrauterine device (IUD) may be inserted within 5 days of coitus.

b. Mechanism of action: Mixed hormonal or progestin-only methods work by interfering with or delaying ovulation and do not interfere with established pregnancy. Ulipristal, likewise, works by delaying ovulation, but it may result in first-trimester fetal loss.

c. Guidelines and instructions for use:

- (1) Counseling about EC should be a routine part of anticipatory guidance for all female and male adolescents. Levonorgestrel methods are available over the counter—no prescription necessary—but must be requested directly from the pharmacist by persons aged 17 or older in all 50 states. Advance prescriptions should be considered for all teens aged 16 and younger, regardless of current sexual activity. Ulipristal requires a prescription regardless of patient age.
- (2) EC should be taken as soon as possible; there is a linear relationship between efficacy and the time from intercourse to treatment.
- (3) If using progestin or mixed hormonal EC, taking the EC dose should not be delayed for pregnancy test, given diminishing efficacy over time to dosing. However, possibility of pregnancy *must* be excluded before ulipristal dosing.
- (4) Discuss proper use of regular, reliable birth control for the future, especially for patients frequently using EC.
- (5) May be combined with other ongoing methods of birth control.
  - (a) OCPs may be started 24 hours after progestin-only or combined hormonal EC dosing has been completed. DMPA may be given the same day.
  - (b) Expert opinion varies regarding initiation of hormonal contraception after ulipristal use (from 7–14 days); a barrier method should be used for the remainder of the cycle.
- (6) No absolute limit of EC frequency during a cycle.
- (7) Perform pregnancy test if no menses within 3 weeks of progestin-only or combined hormonal methods, or if menses more than 1 week late with ulipristal.
- (8) Advise patients to schedule a primary care medical visit after EC usage (pregnancy test and appropriate STI testing or treatment).

d. Contraindications:

- (1) For progestin-only regimens: Pregnancy, given lack of efficacy with potential for side effects; no evidence of teratogenicity.
- (2) For ulipristal: Pregnancy, given potential for first-trimester fetal loss; no evidence of teratogenicity.

- (3) For estrogen-containing regimens: Same as those for OCPs, but use over time has shown that such stringent restrictions for single use are unnecessary. History of previous thrombosis is not a contraindication for single use, but progestin-only methods are preferred.

#### D. Follow-up Recommendations<sup>8</sup>

Two or three follow-up visits per year to monitor patient compliance, blood pressure, and side effects

#### E. Vaginal Infections, Genital Ulcers, and Warts<sup>16</sup>

See Chapter 17 for discussion of infection with chlamydia, gonorrhea, pelvic inflammatory disease, syphilis, and HIV. See Formulary for treatment dosage information. After diagnosis of STI, encourage patient to refrain from intercourse until full therapy is complete, partner is treated, and all visible lesions are resolved.

1. **Diagnostic features of vaginal infections** (Table 5-3) can assist in differentiating normal vaginal discharge from bacterial vaginosis, trichomoniasis, and yeast vaginitis.
2. **Diagnostic features of various genital lesions**, as well as management of warts and ulcers, are presented in Table 5-4.

### VI. MENTAL HEALTH

#### A. Anxiety, Depression, and Bipolar Disorder

Please refer to Disorders of Mental Health, Chapter 9, Section IX.

#### B. Suicidality<sup>30</sup>

1. **Suicide is a leading cause of mortality among adolescents.** Risk factors include male sex, American Indian/Alaska Native racial background, bisexual or homosexual orientation, isolation or living alone, history of acute stressor or recent loss, family history of suicide, personal or family history of suicide attempt, personal or parental mental health problems, physical or sexual abuse, substance use, and firearms in the home (even if properly stored and secured).
2. **Screening questions for suicidal ideation are best asked after initial questioning regarding stressors, mood, and depressive symptoms.** Remember that irritability, vague or multiple somatic complaints, and behavioral problems may indicate depression in an adolescent.
3. **In addition to risk factors above**, assessment of suicidal risk should also include whether the adolescent has a plan, the potential lethality of the plan, access to means to carry out the plan, and whether the plan has ever been rehearsed.
4. **Any adolescent with risk factors and a suicide plan should be considered an imminent risk and not be allowed to leave the office.** Providers should contact local crisis support resources and undertake immediate consultation with a mental health professional; potential courses of action must

TABLE 5-3

## DIAGNOSTIC FEATURES AND MANAGEMENT OF VAGINAL INFECTIONS

	No Infection	Yeast Vaginitis	Trichomoniasis	Bacterial Vaginosis
Etiology	—	<i>Candida albicans</i> and other yeasts	<i>Trichomonas vaginalis</i>	<i>Gardnerella vaginalis</i> , anaerobic bacteria, mycoplasma
Typical symptoms	None	Vulvar itching, irritation, ↑ discharge	Malodorous frothy discharge, vulvar itching	Malodorous, slightly ↑ discharge
Discharge				
Amount	Variable; usually scant	Scant to moderate	Profuse	Moderate
Color*	Clear or white	White	Yellow-green	Usually white or gray
Consistency	Nonhomogenous, floccular	Clumped; adherent plaques	Homogenous	Homogenous, low viscosity; smoothly coats vaginal walls
Vulvar/vaginal inflammation	No	Yes	Yes	No
pH of vaginal fluid†	Usually < 4.5	Usually < 4.5	Usually > 5.0	Usually > 4.5
Amine ("fishy") odor with 10% potassium hydroxide (KOH)	None	None	May be present	Present
Microscopy‡	Normal epithelial cells; <i>Lactobacillus</i> predominates	Leukocytes, epithelial cells, yeast, mycelia, or pseudomycelia in 40%–80% of cases	Leukocytes; motile trichomonads seen in 50%–70% of symptomatic patients, less often if asymptomatic	Clue cells, few leukocytes; <i>Lactobacillus</i> outnumbered by profuse mixed flora (nearly always including <i>G. vaginalis</i> plus anaerobes)
Usual treatment (see Formulary)	None	Oral fluconazole; intravaginal azoles	Metronidazole or tinidazole	Oral/intravaginal metronidazole or clindamycin
Management of sex partners	None	None	Treatment recommended	None

\*Color of discharge is determined by examining vaginal discharge against the white background of a swab.

†pH determination is not useful if blood is present.

‡To detect fungal elements, vaginal fluid is digested with 10% KOH before microscopic examination; to examine for other features, fluid is mixed (1:1) with physiologic saline.

**NOTE:** Refer to Formulary for dosing information.

From Workowski KA, Berman S. Sexually transmitted diseases treatment guidelines, 2010. *MMWR Recomm Rep*. 2010;59(RR-12):1-110.

TABLE 5-4

## DIAGNOSTIC FEATURES AND MANAGEMENT OF GENITAL ULCERS AND WARTS

Infection	Clinical Presentation	Presumptive Diagnosis	Definitive Diagnosis	Treatment/Management of Sex Partners
Genital herpes	Grouped vesicles, painful shallow ulcers	Tzanck preparation with multinucleated giant cells	HSV PCR	No known cure. Prompt initiation of therapy shortens duration of first episode. For severe recurrent disease, initiate therapy at start of prodrome or within 1 day. Transmission can occur during asymptomatic periods. See Formulary for dosing of acyclovir, famciclovir, or valacyclovir.
Chancroid	Etiology: <i>Haemophilus ducreyi</i> Painful genital ulcer; tender, suppurative inguinal adenopathy	No evidence of <i>Treponema pallidum</i> (syphilis) on darkfield microscopy or serologic testing; negative HSV	Use of special media (not widely available in United States); sensitivity < 80%	Single dose: Azithromycin 1 g orally OR Ceftriaxone 250 mg IM Partners should be examined and treated, regardless of whether symptoms are present, or if they have had sex within 10 days preceding onset of patient's symptoms. Syphilis is a common copathogen with chancroid.
Primary syphilis	Indurated, well-defined, usually single painless ulcer or chancre; nontender inguinal adenopathy	Nontreponemal serologic test: VDRL, RPR, or STS	Treponemal serologic test: FTA-ABS or MHA-TP; dark-field microscopy or direct fluorescent antibody tests of lesion exudates or tissue	Parenteral penicillin G (see Chapter 17 for preparation(s), dosage, and length of treatment.) Treat presumptively for persons exposed within 3 months preceding the diagnosis of primary syphilis in a sex partner or who were exposed >90 days preceding the diagnosis and in whom serologic tests may not be immediately available or follow-up is uncertain.

Continued

TABLE 5-4

## DIAGNOSTIC FEATURES AND MANAGEMENT OF GENITAL ULCERS AND WARTS—(Continued)

Infection	Clinical Presentation	Presumptive Diagnosis	Definitive Diagnosis	Treatment/Management of Sex Partners
HPV infection (genital warts)	Single or multiple soft, fleshy, papillary or sessile, painless growths around anus, vulvovaginal area, penis, urethra, or perineum; no inguinal adenopathy	Typical clinical presentation	Papanicolaou smear revealing typical cytologic changes	Treatment does not eradicate infection. Goal: Removal of exophytic warts. Exclude cervical dysplasia before treatment. Patient-administered therapies include podofilox and imiquimod cream. Clinician-applied therapies include podophyllin 10%–25% in compound tincture of benzoin, bichloroacetic or trichloroacetic acid, surgical removal, and cryotherapy with liquid nitrogen or cryoprobe. Podofilox, imiquimod, and podophyllin are contraindicated in pregnancy. Period of communicability unknown.

**NOTE:** Chancroid, lymphogranuloma venereum (LGV), and granuloma inguinale should be considered in the differential diagnosis of genital ulcers if the clinical presentation is atypical and tests for herpes and syphilis are negative.

FTA-ABS, Fluorescent treponemal antibody absorbed; HPV, human papillomavirus; HSV, herpes simplex virus; IM, intramuscular; MHA-TP, microhemagglutination assay for antibody to *Treponema pallidum*; RPR, rapid plasma reagin; STS, serologic test for syphilis; VDRL, Venereal Disease Research Laboratory.

Modified from Workowski KA, Berman S. Sexually transmitted diseases treatment guidelines, 2010. *MMWR Recomm Rep*. 2010;59(RR-12):1-110.

be individualized but include same-day mental health appointment, transfer to a psychiatric emergency room, and psychiatric hospitalization.

5. **Any adolescent with risk factors but no suicide plan or preparation should be considered moderate risk.** He or she should be provided with an immediate plan for behavioral health treatment, information about emergency resources, and ideas for coping strategies.

### C. School Problems

Please refer to Chapter 9 for more information on learning disabilities (Medical Evaluation of Developmental Disorders) and attention deficit hyperactivity disorder (ADHD) (see Table 9-7).

### D. Substance Use<sup>29</sup>

1. **Spectrum of substance use behavior:** Ranges from experimentation to limited use to dependence
2. **Drugs of abuse and acute toxidromes:** See Chapter 2
3. **Screening, brief intervention, and referral to treatment (SBIRT)**
  - a. **Substance use screening:** Any alcohol, marijuana, other drugs in the past 12 months? If yes, administer full CRAFFT questionnaire (see [Box 5-2](#)). If no, administer only "Car" question (Ever ridden in a car with a driver who had used alcohol or drugs?)
  - b. **Brief Intervention:** stratify risk based on responses to screening questions.
    - (1) Low risk (abstinent): Reinforce decisions with praise and anticipatory guidance regarding riding in a car with a driver under the influence.
    - (2) Yes to "Car" question: Counsel, encourage safety plan, consider Contract for Life (<http://www.sadd.org/contract.htm>).
    - (3) Moderate risk (CRAFFT negative): Advise to stop using the substance, educate regarding health risks of continued use, praise personal attributes.
    - (4) High risk (CRAFFT  $\geq 2$ ): Conduct in-depth assessment using motivational enhancement techniques, conduct brief negotiated interview, or refer as appropriate.
  - c. **Referral to Treatment:** Further evaluation by a specialist in mental health/addiction can guide referral to an appropriate level of care.
4. **Levels of care**
  - a. Substance use treatment may be delivered in a variety of settings, ranging from outpatient therapy to partial hospital to inpatient or residential treatment.
  - b. Considerations for detoxification: Medical management of symptoms of withdrawal, particularly pertinent to teens dependent on alcohol, opioids, or benzodiazepines. **NOTE:** Detoxification is not equivalent to substance abuse treatment; once acute withdrawal symptoms have been managed, engage patient in a treatment program.

## VII. TRANSITIONING ADOLESCENTS INTO ADULT CARE

All adolescents, particularly those with special healthcare needs or chronic conditions, benefit from careful attention to the process of transitioning

to adult care. Resources for how to approach and organize the transition process are available at [http://www.medicalhomeinfo.org/how/care\\_delivery/transitions.aspx](http://www.medicalhomeinfo.org/how/care_delivery/transitions.aspx).

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# Chapter 6

## Analgesia and Procedural Sedation

Sean Barnes, MD, MBA

 See additional content on Expert Consult

### I. WEB RESOURCES

International Association for the Study of Pain: <http://childpain.org/>

American Pain Society: <http://www.ampainsoc.org/>

American Society of Anesthesiologists: <http://www.asahq.org/>

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### II. PAIN ASSESSMENT

#### A. Infant<sup>1</sup>

1. **Physiologic responses seen primarily in acute pain; subsides with continuing/chronic pain.** Characterized by oxygen desaturation, crying, diaphoresis, flushing or pallor, and increases in blood pressure, heart rate, and respiratory rate.
2. **Behavioral response (Table 6-1):**
  - a. Observe characteristics and duration of cry, facial expressions, visual tracking, body movements, and response to stimuli.
  - b. Neonatal Infant Pain Scale (NIPS): Behavioral assessment tool for the preterm neonate and full-term neonate up to 6 weeks after birth.
  - c. FLACC scale (Table 6-2): Measures and evaluates pain interventions by quantifying pain behaviors like **F**acial expression, **L**eg movement, **A**ctivity, **C**ry, and **C**onsolability, with scores ranging from 0–10.<sup>2</sup> Revised FLACC scale reliable for children with cognitive impairment.<sup>3</sup>

#### B. Preschooler

In addition to physiologic and behavioral responses, the **FACES** pain rating scale can be used to assess pain intensity in children as young as 3 years of age (Fig. 6-1).

#### C. School-Age and Adolescent

Evaluate physiologic and behavioral responses; ask about description, location, and character of pain. Starting at age 7, children can use the standard pain rating scale (0 is no pain and 10 is the worst pain ever experienced).

### III. ANALGESICS

#### A. Nonopioid Analgesics

Weak analgesics with antipyretic activity are commonly used to manage mild to moderate pain of nonvisceral origin. Administer alone or in

**TABLE 6-1**

**DEVELOPMENTAL RESPONSES TO PAIN**

Stage	Age	Response
Infant	<6 mo	No expression of anticipatory fear. Level of anxiety reflects that of the parent.
	6–18 mo	Anticipatory fear of painful experiences begins to develop.
Preschooler	18–24 mo	Verbalization. Children express pain with words such as “hurt” and “boo-boo.”
	3 yr	Localization and identification of external causes. Children more reliably assess their pain but continue to depend on visual cues for localization and are unable to understand a reason for pain.
School-age child	5–7 yr	Cooperation. Children have improved understanding of pain and ability to localize it and cooperate.

Data from Yaster, M, et al. Cognitive Development Aspects of Pain in School-Age Children. *Pain In Infants, Children, and Adolescents*. 1993; 65-74.

**TABLE 6-2**

**FLACC PAIN ASSESSMENT TOOL**

<b>FACE</b>
0—No particular expression or smile
1—Occasional grimace or frown, withdrawn, disinterested
2—Frequent to constant frown, quivering chin, clenched jaw
<b>LEGS</b>
0—Normal position or relaxed
1—Uneasy, restless, tense
2—Kicking or legs drawn up
<b>ACTIVITY</b>
0—Lying quietly, normal position, moves easily
1—Squirming, shifting back and forth, tense
2—Arched, rigid, or jerking
<b>CRY</b>
0—No cry (awake or asleep)
1—Moans or whimpers, occasional complaint
2—Crying steadily, screams or sobs, frequent complaints
<b>CONSOLABILITY</b>
0—Content, relaxed
1—Reassured by occasional touching, hugging, or being talked to; distractible
2—Difficult to console or comfort

Modified from Manworren R, Hynan L. Clinical validation of FLACC: preverbal patient pain scale. *Pediatr Nurs*. 2003;29:140-146.

combination with opiates. Drugs, routes of administration, and specific comments are as follows:

1. **Acetaminophen (by mouth [PO]/per rectum [PR]/intravenous [IV]):** Weak analgesic with no anti-inflammatory activity; no platelet inhibition or gastrointestinal (GI) irritation. Hepatotoxicity with high doses.
2. **Aspirin (PO/PR):** Associated with platelet inhibition and GI irritation. Avoid in pediatrics, owing to risk of Reye syndrome.

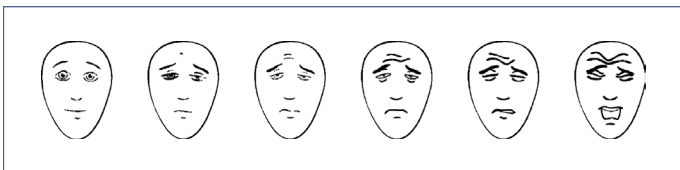


FIGURE 6-1

Faces pain scale. (From Hicks CL, von Baeyer CL, Spafford PA, et al. The Faces Pain Scale-Revised: toward a common metric in pediatric pain measurement. *Pain*. 2001;93:173-183. With instructions and translations as found on the website: <http://www.usask.ca/childpain/fpsr/>. This Faces Pain Scale-Revised has been reproduced with permission of the International Association for the Study of Pain [IASP]. The figure may not be reproduced for any other purpose without permission.)

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3. **Choline magnesium trisalicylate (PO):** No platelet inhibition. Also associated with Reye syndrome.
4. **Nonsteroidal anti-inflammatory drugs (NSAIDs):** Ibuprofen (PO), ketorolac (IV/intramuscular [IM]/PO), naproxen (PO)
  - a. Especially useful for sickle cell, bony, rheumatic, and inflammatory pain
  - b. Associated with GI symptoms (epigastric pain, gastritis, GI bleeding): Recommend histamine-2-receptor blocker concurrently with prolonged use
  - c. Other adverse effects: Interference with platelet aggregation, bronchoconstriction, hypersensitivity reactions, and azotemia. May interfere with bone healing. Should be avoided in patients with severe renal disease, dehydration, or heart failure.

**NOTE:** Ketorolac is a potent analgesic (1 mg/kg IV is equivalent to 0.1 mg/kg morphine). Only parenteral NSAID available.

See the quick reference to analgesics drugs in Table EC 6-A on Expert Consult.

## B. Opioids (Table 6-3)

1. **Produce analgesia by binding mu receptors in the brain and spinal cord**
2. **Most flexible and widely used analgesics for moderate and severe pain**
3. **Side effects:** Pruritus, nausea, vomiting, constipation, urine retention, and (rarely) respiratory depression and hypotension
4. **Morphine:** Gold standard of this drug class

## C. Local Anesthetics<sup>4-7</sup>

Administered topically or subcutaneously into peripheral nerves (e.g., digital nerve, penile nerve block) or centrally (epidural/spinal). They act by temporarily blocking nerve conduction at the sodium channel.

1. **For all local anesthetics, 1% solution = 10 mg/mL**
2. **Topical local anesthetics (Table 6-4)<sup>8</sup>**
3. **Injectable local anesthetics (Table 6-5):**
  - a. Infiltration of the skin at the site: Used for painful procedures such as wound closure, IV line placement, or lumbar puncture

TABLE EC 6-A

## ANALGESICS AND SEDATIVE-HYPNOTIC DRUGS QUICK REFERENCE (ALPHABETICAL)

Drug	Route	Dose
<b>SEDATIVE-HYPNOTIC</b>		
Diazepam	PO IV (painful)	0.25–0.3 mg/kg 0.1 mg/kg; max 0.6 mg/kg within 8 hours
Dexmedetomidine	IN	1–2 mcg/kg
Diphenhydramine	PO, IV, IM	1 mg/kg; max 50 mg/dose
Hydroxyzine	PO  IM	2 mg/kg/day divided Q6–8 hr; max dose 600 mg/24 hr  0.5–1 mg/kg/dose Q4–6 hr; max dose 600 mg/24 hr
Lorazepam	PO, IV, IM	0.05 mg/kg; max 2 mg/dose
Midazolam	PO  PR IN IM IV sedation	0.5–0.8 mg/kg; max 20 mg/ dose  0.5–1 mg/kg 0.2–0.3 mg/kg 0.15–0.2 mg/kg 0.1 mg/kg; max 10 mg/total dose
<b>ANALGESIC</b>		
Acetaminophen	PO, PR, IV	10–15 mg/kg Q4–6 hr (if >50 kg, 650–1000 mg Q4–6 hr)
Fentanyl	IV IV infusion PO oralet IN	1 mcg/kg 1–5 mcg/kg/hr 10–15 mcg/kg; max 400 mcg 1 mcg/kg
Hydrocodone*	PO	0.135 mg/kg Q4–6 hr; max 2 mg/dose
Hydromorphone	IV IV infusion	0.015 mg/kg; max 2 mg/dose 2–4 mcg/kg/hr
Ketorolac	IV, IM	0.5 mg/kg Q6hr; max 30 mg/dose
Methadone	PO, IV, IM, SQ	0.1 mg/kg Q8–12 hr; max 10 mg/dose
Morphine	IV  IV infusion	0.05–0.2 mg/kg; max 15 mg/dose 10–40 mcg/kg/hr
Oxycodone	PO	0.1 mg/kg Q4–6 hr; max 5 mg/dose
<b>OTHER</b>		
Ketamine	PO IV IM	5 mg/kg 0.25–2 mg/kg 2–5 mg/kg

\*Commonly with acetaminophen.

IM, Intramuscular; IN, intranasal; IV, intravenous; PO, by mouth; PR, per rectum; SQ, subcutaneous.

Data from Fisher QA. *Pediatric Anesthesia Pearls*. Baltimore: Johns Hopkins Department of Anesthesia and Critical Care Medicine, 2000.

TABLE 6-3

## COMMONLY USED OPIATES

Drug	Route; Equi-analgesic Doses (mg/kg/dose)	Onset (min)	Duration (hr)	Side Effects	Comments
Codeine	PO; 1.2	30–60	3–4	<ul style="list-style-type: none"> <li>• Can cause severe nausea and vomiting</li> <li>• Histamine release</li> </ul>	<b>No longer recommended in pediatrics;</b> 3%–5% of population overmetabolize, potentially leading to catastrophic overdose. Converted in liver to morphine (10%). Newborns and 10% of U.S. population cannot make this conversion.
Fentanyl	IV; 0.001	1–2	0.5–1	<ul style="list-style-type: none"> <li>• Pruritus</li> <li>• Bradycardia</li> <li>• Chest wall rigidity with doses &gt;5 mcg/kg (but can occur at all doses); treat with naloxone or neuromuscular blockade</li> </ul>	Rarely causes cardiovascular instability (relatively safer in hypovolemia, congenital heart disease, or head trauma).
	Transdermal; 0.001	12	2–3		Respiratory depressant effect much longer (4 hr) than analgesic effect. Levels of unbound drug are higher in newborns.
	Transmucosal; 0.01	15			Most commonly used opioid for short, painful procedures, but transdermal route is more effective in chronic pain situations.
Hydromorphone	IV/SQ; 0.015	5–10	3–4		Less sedation, nausea, pruritus than morphine.
	PO; 0.02–0.1	30–60			
Methadone	IV; 0.1	5–10	4–24		Initial dose may produce analgesia for 3–4 hr; duration of action is increased with repeated dosing.
	PO; 0.1	30–60	4–24		
Morphine	IV; 0.1	5–10	3–4	<ul style="list-style-type: none"> <li>• Seizures in neonates</li> <li>• Can cause significant histamine release</li> </ul>	The gold standard against which all other opioids are compared. Available in sustained-release form for chronic pain.
	IM/SQ; 0.1–0.2	10–30	4–5		
	PO; 0.3–0.5	30–60	4–5		
Oxycodone	PO; 0.1	30–60	3–4		Available in sustained-release form for chronic pain. Much less nauseating than codeine.

IM, Intramuscular; IV, intravenous; PO, by mouth; SQ, subcutaneous.

Modified from Yaster M, Cote C, Krane E, et al. *Pediatric Pain Management and Sedation Handbook*. St Louis: Mosby, 1997:29–50.

TABLE 6-4

COMMONLY USED TOPICAL LOCAL ANESTHETICS<sup>8</sup>

	Components	Indications	Peak Effect	Duration*	Cautions†
EMLA	Lidocaine 2.5% Prilocaine 2.5%	Intact skin only Venipuncture, circumcision, LP, abscess drainage, BMA	60 min	90 min	Methemoglobinemia: not for use in patients predisposed to methemoglobin- emia (e.g., G6PD deficiency, some medications) Infants <3 mo of age: use sparingly (up to 1 g is safe)
LMX	Lidocaine 4%	Same as EMLA	30 min	60 min	Same as EMLA
LET	Lidocaine 4% Epinephrine 0.1% Tetracaine 0.5% Can be mixed with cellulose to create a gel	Safe for nonintact skin Lacerations Not for use in contaminated wounds	30 min	45 min	Vasoconstriction: contraindicated in areas supplied by endarteries (e.g., pinna, nose, penis, digits) Avoid contact with mucus membranes
Viscous lidocaine	Lidocaine 2% May be mixed with Maalox and Benadryl elixir in a 1:1:1 ratio for palatability	Safe for nonintact skin Mucous mem- branes (e.g., urethral cath- eter placement, mucositis)	10 min	30 min	Overuse can lead to life-threatening toxicity Not to be used for teething

\*Approximate.

†Maximum lidocaine dose is 5 mg/kg.

BMA, Bone marrow aspiration; EMLA, eutectic mixture of local anesthetics; G6PD, glucose-6-phosphate dehydrogenase; LP, lumbar puncture.

TABLE 6-5

COMMONLY USED INJECTABLE LOCAL ANESTHETICS<sup>1,5</sup>

Agent	Concentration (%) (1% solution = 10 mg/mL)	Max dose (mg/kg)	Onset (min)	Duration (hr)
Lidocaine	0.5–2	5	3	0.5–2
Lidocaine with epinephrine	0.5–2	7	3	1–3
Bupivacaine	0.25–0.75	2.5	15	2–4
Bupivacaine with epinephrine	0.25–0.75	3	15	4–8
Ropivacaine	0.2–0.5	3.5	15	2–4

NOTE: Max volume = (max mg/kg × weight in kg)/(% solution × 10).

Data from St Germain Brent A. The management of pain in the emergency department. *Pediatr Clin North Am.* 2000;47:651–679; and Yaster M, Cote C, Krane E, et al. *Pediatric Pain Management and Sedation Handbook*. St Louis: Mosby, 1997:51–72.

- b. To reduce stinging from injection, use a small needle (27- to 30-gauge). Alkalinize anesthetic: Add 1 mL (1 mEq) sodium bicarbonate to 9 mL lidocaine (or 29 mL bupivacaine), use lowest concentration of anesthetic available, warm solution (between 37° and 42° C), inject anesthetic slowly, and rub skin at injection site first.
- c. To enhance efficacy and duration, add epinephrine to decrease vascular uptake. **Never use local anesthetics with epinephrine in areas supplied by end arteries (e.g., pinna, digits, nasal tip, penis).**
- d. Toxicity: Central nervous system (CNS) and cardiac toxicity are of greatest concern. CNS symptoms are seen before cardiovascular collapse. Progression of symptoms: Perioral numbness, dizziness, auditory disturbances, muscular twitching, unconsciousness, seizures, coma, respiratory arrest, cardiovascular collapse. It is important to calculate the volume limit of the local anesthetic and always draw up less than the maximum volume (see Formulary for maximum doses). Lipid emulsion therapy and possibly cardiopulmonary bypass may be required for systemic toxicity. If concerned for systemic toxicity, please contact an anesthesiologist.  
**NOTE:** Bupivacaine is associated with more severe cardiac toxicity than lidocaine.

#### **D. Nonpharmacologic Measures of Pain Relief<sup>9,10</sup>**

1. **Sucrose for neonates (Sweet Ease):**
  - a. Indications: Procedures like heel sticks, immunizations, venipuncture, IV line insertion, arterial puncture, insertion of a Foley catheter, and lumbar puncture in neonates and infants. Strongest evidence exists for infants 0–1 month of age,<sup>9</sup> but more recent evidence suggests efficacy up to 12 months.<sup>10</sup>
  - b. Procedure: administer up to 2 mL of 24% sucrose into the infant's mouth by syringe or from a nipple/pacifier ~ 2 minutes before procedure.  
**NOTE:** Effective doses in very low-birth-weight infants may be as low as 0.05–0.1 mL 24% sucrose, and in term neonates may be as high as 2 mL 24% sucrose.
  - c. May be given for more than one procedure within a relatively short period of time but should not be administered more than twice in 1 hour.  
**NOTE:** Studies have suggested potential adverse neurocognitive effects with many repeated doses.<sup>10</sup>
  - d. Effectiveness has been most often studied with adjunctive pacifier/nipple and parental holding, which may contribute to stress/pain alleviation.
  - e. Avoid use if patient is under nothing by mouth (NPO) restrictions.
2. **Parental presence**
3. **Distraction with toys**
4. **Child life specialists strongly encouraged**

### **IV. PATIENT-CONTROLLED ANALGESIA**

#### **A. Definition**

Patient-controlled analgesia (PCA) is a device that enables a patient to receive continuous (basal) opioids and/or self-administer small supplemental



TABLE 6-6

## ORDERS FOR PATIENT-CONTROLLED ANALGESIA

Drug	Basal Rate (mcg/kg/hr)	Bolus Dose (mcg/kg)	Lockout Period (min)	Boluses (hr)	Max Dose (mcg/kg/hr)
Morphine	10–30	10–30	6–10	4–6	100–150
Hydromorphone	3–5	3–5	6–10	4–6	15–20
Fentanyl	0.5–1	0.5–10	6–10	2–3	2–4

Data from Yaster M, Cote C, Krane E, et al. *Pediatric Pain Management and Sedation Handbook*. St Louis: Mosby, 1997:100.

doses (bolus) of analgesics on an as-needed basis. In children younger than 6 years (or physically/mentally handicapped), a family member, caregiver, or nurse may administer doses (i.e., surrogate PCA, PCA by proxy, or parent/nurse-controlled analgesia).

## B. Indications

Moderate to severe pain of acute or chronic nature. Commonly used in sickle cell disease, postsurgery, posttrauma, burns, and cancer. Also for preemptive pain management (e.g., to facilitate dressing changes).

## C. Routes of Administration

IV, SQ, or epidural

## D. Agents (Table 6-6)

## E. Complications

1. **Pruritus, nausea, constipation, urine retention, excessive drowsiness, respiratory depression.**
2. **Consider a low-dose naloxone (Narcan) infusion (1 mcg/kg/hr) to reduce pruritus and nausea.**

# V. OPIOID TAPERING

## A. Indication

Tapering schedule is required if the patient has received frequent opioid analgesics for >5–10 days, owing to development of dependence and potential for withdrawal.

## B. Withdrawal

1. **See Box 18-1 for symptoms of opiate withdrawal.**
2. **Onset of signs and symptoms:** 6–12 hours after last dose of morphine, 36–48 hours after last dose of methadone.
3. **Duration:** 7–14 days; peak intensity reached within 2–4 days.

## C. Guidelines

1. **Conversion:** Convert all drugs to a single equi-analgesic member of that group (Table 6-7).
2. **PCA wean:** Change drug dosing from continuous/intermittent IV infusion to PO bolus therapy around the clock. If on PCA, administer first PO dose, then stop basal infusion 30–60 minutes later. Keep bolus doses,

TABLE 6-7

## RELATIVE POTENCIES AND EQUIVALENCE OF OPIOIDS

Drug	Morphine Equivalence Ratio	IV Dose (mg/kg)	Equivalent PO Dose (mg/kg)
Meperidine	0.1	1	1.5–2
Methadone	0.25–1*	0.1	0.1
Morphine	1	0.1	0.3–0.5
Hydromorphone	5–7	0.015	0.02–0.1
Fentanyl	80–100	0.001	NA

\*Morphine-to-methadone conversion in tolerant/dependent patient is variable. We recommend starting at the lowest conversion ratio, 0.25.

**NOTE:** Removing a transdermal fentanyl patch does not stop opioid uptake from the skin; fentanyl will continue to be absorbed for 12–24 hr after patch removal (fentanyl 25-mcg patch administers 25 mcg/hr of fentanyl).

IV, Intravenous; NA, not applicable; PO, by mouth.

From Yaster M, Cote C, Krane E, et al. *Pediatric Pain Management and Sedation Handbook*. St Louis: Mosby, 1997:40.

but reduce by 25%–50%. Discontinue PCA if no boluses are required in next 6 hours, increase PO dose, or add adjuvant analgesic (e.g., NSAID).

3. **Slow dose decrease:** During an intermittent IV/PO wean, decrease total daily dose by 10%–20% of original dose every 1–2 days (e.g., to taper a morphine dose of 40 mg/day, decrease the daily dose by 4–8 mg every 1–2 days).
4. **Oral regimen:** If not done previously, convert IV dosing to equivalent PO administration 1–2 days before discharge, and continue titration as outlined previously.
5. **Adjunctive therapy:**  $\alpha_2$ -Agonists (e.g., clonidine, dexmedetomidine)
  - a. Clonidine in combination with opioid has been shown to decrease length of time needed for opioid weaning in neonatal abstinence syndrome, with few short-term side effects. Long-term safety has yet to be thoroughly investigated.<sup>11</sup>
  - b. Limited data exist evaluating use of oral clonidine in iatrogenic opioid abstinence syndrome in critically ill patients, but both transdermal clonidine and dexmedetomidine have shown promise.<sup>12</sup>
  - c. Several studies have examined use of clonidine in treating opioid dependence, but insufficient data exist to support its routine use outside of possibly the neonatal setting.<sup>13</sup>

## D. Examples (Box 6-1)

## VI. PROCEDURAL SEDATION<sup>1,4-7,14</sup>

### A. Definitions

1. **Mild sedation (anxiolysis):** Intent is anxiolysis with maintenance of consciousness. Practically, obtained when a single drug is given once at a low dose (not chloral hydrate). Mild sedation can easily progress to deep sedation and general anesthesia.

## BOX 6-1

## EXAMPLES OF OPIOID TAPERING

## EXAMPLE 1

Patient on morphine patient-controlled analgesia (PCA) to be converted to oral (PO) morphine with home weaning.

For example: morphine PCA basal rate = 2 mg/hr, average bolus rate = 0.5 mg/hr

Step 1: Calculate daily dose: basal + bolus =  $(2 \text{ mg/hr} \times 24 \text{ hr}) + (0.5 \text{ mg/hr} \times 24 \text{ hr}) = 60 \text{ mg}$  intravenous (IV) morphine

Step 2: Convert according to drug potency: morphine IV/morphine oral = approx 3:1 potency;  $3 \times 60 \text{ mg} = 180 \text{ mg}$  PO morphine

Step 3: Prescribe 90 mg BID or 60 mg TID; wean 10%–20% of original dose (30 mg) every 1–2 days

## EXAMPLE 2

Patient on morphine PCA to be converted to transdermal fentanyl. Morphine PCA basal rate = 2 mg/hr. No boluses.

Step 1: Convert according to drug potency: fentanyl/morphine = approx 100:1 potency;  $2 \text{ mg/hr morphine} = 2000 \text{ mcg/hr morphine} = 20 \text{ mcg/hr fentanyl}$

Step 2: Prescribe 25-mcg fentanyl patch (delivers 25 mcg/hr fentanyl)

Step 3: Stop IV morphine 8 hr after patch is applied; prescribe second patch at 72 hr

Step 4: Prescribe as-needed (PRN) IV morphine with caution

Data from Yaster M, Cote C, Krane E, et al. *Pediatric Pain Management and Sedation Handbook*. St Louis: Mosby, 1997:29-50.

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2. **Moderate sedation:** Formerly known as *conscious sedation*. A controlled state of depressed consciousness during which airway reflexes and airway patency are maintained. Patient responds appropriately to age-appropriate commands (“Open your eyes.”) and light touch. Practically, obtained any time a combination of sedative-hypnotic and analgesic is used. Moderate sedation can easily progress to deep sedation and general anesthesia.
3. **Deep sedation:** A controlled state of depressed consciousness during which airway reflexes and airway patency may not be maintained, and the child is unable to respond to physical or verbal stimuli. Practically, required for most painful procedures in children. The following IV drugs always produce deep sedation: propofol, etomidate, thiopental, methohexital. Deep sedation can progress to general anesthesia.
4. **Dissociative sedation:** Unique state of sedation achieved with ketamine. Deep level of depressed consciousness, but airway reflexes and patency are generally maintained.

See the Quick Reference to Sedative-Hypnotic Drugs in Table EC 6-A.

## B. Preparation

1. Patient should be **NPO** for solids and clear liquids (Table 6-8 shows current American Society of Anesthesiologists recommendations). See Fig. EC 6-A on Expert Consult for more information on fasting recommendations.
2. **Written informed consent**

**Standard-risk patient<sup>a</sup>**

Oral intake in the prior 3 hours	Procedural Urgency			
	<i>Emergent procedure</i>	<i>Urgent procedure</i>	<i>Semi-urgent</i>	<i>Non-urgent</i>
<i>Nothing</i>	All levels of sedation	All levels of sedation	All levels of sedation	All levels of sedation
<i>Clear liquids only</i>	All levels of sedation	All levels of sedation	Up to and including brief deep sedation	Up to and including extended moderate sedation
<i>Light snack</i>	All levels of sedation	Up to and including brief deep sedation	Up to and including dissociative sedation; nonextended moderate sedation	Minimal sedation only
<i>Heavier snack or meal</i>	All levels of sedation	Up to and including extended moderate sedation	Minimal sedation only	Minimal sedation only

**High-risk patient<sup>a</sup>**

Oral intake in the prior 3 hours	Procedural Urgency			
	<i>Emergent procedure</i>	<i>Urgent procedure</i>	<i>Semi-urgent</i>	<i>Non-urgent</i>
<i>Nothing</i>	All levels of sedation	All levels of sedation	All levels of sedation	All levels of sedation
<i>Clear liquids only</i>	All levels of sedation	Up to and including brief deep sedation	Up to and including extended moderate sedation	Minimal sedation only
<i>Light snack</i>	All levels of sedation	Up to and including dissociative sedation; nonextended moderate sedation	Minimal sedation only	Minimal sedation only
<i>Heavier snack or meal</i>	All levels of sedation	Up to and including dissociative sedation; nonextended moderate sedation	Minimal sedation only	Minimal sedation only

**Procedural sedation and analgesia targeted depth and duration**

← Increasing potential aspiration risk ↓	Minimal sedation only
	Dissociative sedation; brief or intermediate-length moderate sedation
	Extended moderate sedation
	Brief deep sedation
	Intermediate or extended-length deep sedation

Brief: <10 minutes  
 Intermediate: 10–20 minutes  
 Extended: >20 minutes

<sup>a</sup>Higher-risk patients (one or more of the following): Potential for difficult or prolonged assisted ventilation should an airway complication occur; conditions predisposing to esophageal reflux; extremes of age (e.g., >70 years or <6 months); American Society of Anesthesiologists (ASA) physical status 3 or greater; other concerning clinical findings.

**FIGURE EC 6-A**

Prudent limits of targeted depth and length of emergency department procedural sedation and analgesia according to presedation assessment of aspiration risk. (From Green SM, Roback MG, Miner JR, et al. Fasting and emergency department procedural sedation and analgesia: a consensus-based clinical practice advisory. *Ann Emerg Med.* 2007;49:454-461.)

**TABLE 6-8****FASTING RECOMMENDATIONS FOR ANESTHESIA**

Food Type	Minimum Fasting Period (hr)
Clear liquids	2
Breast milk	4
Nonhuman milk, formula	6
Solids	8

Data from Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures. A report by the American Society of Anesthesiologists Task Force on Preoperative Fasting and Use of Pharmacologic Agents to Reduce the Risk of Pulmonary Aspiration [Online]. <http://www.asahq.org/publicationsAndServices/NPO.pdf>.

### 3. Focused patient history:

- Allergies and medications
- Airway (asthma, acute respiratory disease, reactive airway disease), airway obstruction (mediastinal mass, history of noisy breathing, obstructive sleep apnea), craniofacial abnormalities (e.g., Pfeiffer, Crouzon, Apert, Pierre Robin syndromes), recent upper respiratory infection (suggests increased risk of laryngospasm)
- Aspiration risk (neuromuscular disease, esophageal disease, altered mental status, obesity, pregnancy)
- Prematurity, comorbidities, and adverse reactions to sedatives and anesthesia

### 4. Physical examination:

With specific attention to head, ears, eyes, nose, and throat (HEENT); lungs; cardiac examination; and neuromuscular function. Assess ability to open mouth and extend neck. If risk for moderate sedation is too high, consider an anesthesia consultation and general anesthesia.

### 5. Determine American Society of Anesthesiologists Physical Status Classification:

See Table EC 6-B on Expert Consult. Class I and II patients are generally good candidates for mild, moderate, or deep sedation outside of the operating room.<sup>15</sup>

### 6. Have an emergency plan ready:

Make sure qualified backup personnel and equipment are close by.

### 7. Personnel:

Two providers are required. One provider should perform the procedure, and a separate provider should monitor the patient during sedation and recovery.

### 8. Ensure IV access.

### 9. Have airway/intubation equipment available

(see Chapter 1).

### 10. Medications

to have available: Those for rapid sequence intubation (see Chapter 1) or emergencies (e.g., epinephrine, atropine)

### 11. Antagonist (reversal) agents

should be readily available (e.g., naloxone, flumazenil).

## C. Monitoring

### 1. Vital signs:

Obtain baseline vital signs (including pulse oximetry). Continuously monitor heart rate and oxygen saturation; intermittently monitor

TABLE EC 6-B

**AMERICAN SOCIETY OF ANESTHESIOLOGISTS PHYSICAL STATUS CLASSIFICATION<sup>10</sup>**

Class I	A normally healthy patient
Class II	A patient with mild systemic disease (e.g., controlled reactive airway disease)
Class III	A patient with severe systemic disease (e.g., a child who is actively wheezing)
Class IV	A patient with severe systemic disease that is a constant threat to life (e.g., a child with status asthmaticus)
Class V	A moribund patient who is not expected to survive without the operation (e.g., a patient with severe cardiomyopathy requiring heart transplantation)

blood pressure and respiratory rate. Record vital signs at least every 5 minutes until patient returns to presedation level of consciousness.

**NOTE:** Complications most often occur 5–10 minutes after administration of IV medication and immediately after a procedure is completed (when stimuli associated with the procedure are removed).<sup>7</sup>

2. **Airway:** Frequently assess airway patency and adequacy of ventilation through capnography, auscultation, or direct visualization.

#### D. Pharmacologic Agents

1. **Goal of sedation:** To tailor drug combination to provide levels of analgesia, sedation-hypnosis, and anxiolysis deep enough to facilitate procedure but shallow enough to avoid loss of airway reflexes.
2. **CNS, cardiovascular, and respiratory depression** are potentiated by combining sedative drugs and/or opioids and by rapid drug infusion. Titrate to effect.
3. **Common sedative/hypnotic agents** (Box 6-2):  
Also see Tables 6-3 and 6-9 for more information on opiates and barbiturates/benzodiazepines.

#### BOX 6-2

##### PROPERTIES OF COMMON SEDATIVE-HYPNOTIC AGENTS

###### SEDATING ANTIHISTAMINES (DIPHENHYDRAMINE, HYDROXYZINE)

- Mild sedative-hypnotics with antiemetic and antipruritic properties; used for sedation and treatment of opiate side effects
- No anxiolytic or analgesic effects

###### BARBITURATES

- Contraindicated in patients with porphyria; suitable only for nonpainful procedures.
- No anxiolytic or analgesic effects

###### BENZODIAZEPINES

- Reversible with flumazenil.
- + Anxiolytic effects; no analgesic effects

###### OPIOIDS

- Reversible with naloxone
- + Analgesic effects; no anxiolytic effects

###### KETAMINE<sup>1,5,9</sup>

- Phencyclidine derivative that causes potent dissociative anesthesia, analgesia, and amnesia
- Nystagmus indicates likely therapeutic effect
- Vocalizations/movement may occur even with adequate sedation
- Results in “dissociative sedation” by any route
- Onset: IV, 0.5–2 min; IM, 5–10 min; PO/PR, 20–45 min
- Duration: IV, 20–60 min; IM, 30–90 min; PO/PR, 60–120+ min
- **CNS effects:** Increased ICP, emergence delirium with auditory, visual, and tactile hallucinations
- **Cardiovascular effects:** Inhibits catecholamine reuptake, causing increased HR, BP, SVR, PVR, direct myocardial depression

*Continued*

## BOX 6-2

## PROPERTIES OF COMMON SEDATIVE-HYPNOTIC AGENTS (Continued)

## KETAMINE (Continued)

- **Respiratory effects:** Bronchodilation (useful in asthmatics), increased secretions (can result in laryngospasm), maintenance of ventilatory response to hypoxia, relative maintenance of airway reflexes
- **Other effects:** Increased muscle tone, myoclonic jerks, increased IOP, nausea, emesis
- **Contraindications:** Increased ICP, increased IOP, hypertension, preexisting psychotic disorders

## PROPOFOL

- For purpose of deep sedation or general anesthesia, give 0.5–1 mg/kg IV bolus, followed by 50–100 mcg/kg/min infusion
- Rapid onset and brief recovery (5–15 min), antiemetic, and euphoric
- Caution: Respiratory depression, apnea, hypotension
- + Anxiolytic. No analgesic effects

## DEXMEDETOMIDINE\*

- Give 0.5–2 mcg/kg IV load over 10 min, followed by 0.2–1 mcg/kg/hr infusion.
- Extremely rapid onset and brief recovery (5–15 min) antiemetic and euphoric.
- Does not cause respiratory depression or apnea.
- + Anxiolytic and analgesic effects.
- Dexmedetomidine can also be given intranasally (1–2 mcg/kg). It will take 30–60 min to attain natural sleep, and patients will briefly awaken with stimulation. Can cause hypotension and bradycardia. Increased cost compared with other medications.

## DEXMEDETOMIDINE AND KETAMINE\*

- Most effective regimen appears to be use of bolus dose of both agents, dexmedetomidine (1 mcg/kg) and ketamine (1–2 mg/kg), to initiate sedation.
- This can then be followed by a dexmedetomidine infusion (1–2 mcg/kg/hr) with supplemental bolus doses of ketamine (0.5–1 mg/kg) as needed.

\*These examples reflect commonly used current protocols at the Johns Hopkins Children's Center; variations are found at other institutions. See Formulary for dosing recommendations.

BP, Blood pressure; CNS, central nervous system; HR, heart rate; ICP, intracranial pressure; IM, intramuscular; IOP, intraocular pressure; IV, intravenous; PO, oral; PR, rectal; PVR, pulmonary vascular resistance; SVR, systemic vascular resistance.

Data from Yaster M, Cote C, Krane E, et al. *Pediatric Pain Management and Sedation Handbook*. St Louis: Mosby, 1997:376–382; St Germain Brent A. The management of pain in the emergency department. *Pediatr Clin North Am*. 2000;47:651–679; and Cote CJ, Lerman J, Todres ID, et al. *A Practice of Anesthesia for Infants and Children*. Philadelphia: WB Saunders, 2001.

## 4. Reversal agents:

- a. Naloxone: Opioid antagonist. See [Box 6-3](#) for Narcan administration protocol.
- b. Flumazenil: Benzodiazepine antagonist. See Formulary for dosing details.

E. Discharge Criteria<sup>15</sup>

1. **Airway is patent and cardiovascular function is stable.**
2. **Easy arousability; intact protective reflexes (swallow and cough, gag reflex).**



TABLE 6-9

COMMONLY USED BENZODIAZEPINES\* AND BARBITURATES<sup>1,5,14</sup>

Drug Class	Duration of Action	Drug	Route	Onset (min)	Duration (hr)	Comments
Benzodiazepines	Short	Midazolam (Versed)	IV	1–3	1–2	<ul style="list-style-type: none"> <li>• Has rapid and predictable onset of action, short recovery time</li> <li>• Causes amnesia</li> <li>• Results in mild depression of hypoxic ventilatory drive</li> <li>• Poor choice for procedural sedation</li> <li>• Excellent for muscle relaxation or prolonged sedation</li> <li>• Painful on IV injection</li> <li>• Faster onset than midazolam</li> <li>• Poor choice for procedural sedation</li> <li>• Ideal for prolonged anxiolysis, seizure treatment</li> </ul>
			IM/IN	5–10		
			PO/PR	10–30		
	Intermediate	Diazepam (Valium)	IV (painful)	1–3	0.25–1	
			PR	7–15	2–3	
			PO	30–60	2–3	
	Long	Lorazepam (Ativan)	IV	1–5	3–4	
			IM	10–20	3–6	
			PO	30–60	3–6	
Barbiturates	Short	Methohexital	PR†	5–10	1–1.5	<ul style="list-style-type: none"> <li>• PR form used as sedative for nonpainful procedures</li> <li>• Predictable sedation and immobility for nonpainful procedures</li> <li>• Minimal respiratory depression when used alone</li> <li>• Associated with slow wake up and agitation</li> </ul>
	Intermediate	Pentobarbital	IV	1–10	1–4	
			IM	5–15	2–4	
			PO/PR	15–60	2–4	

\*Use IV solution for PO, PR, and IN administration. Rectal diazepam gel (Diastat) is also available.

†IV administration produces general anesthesia; only PR should be used for sedation.

IM, Intramuscular; IN, intranasal; IV, intravenous; PO, by mouth; PR, per rectum.

Data from Yaster M, Cote C, Krane E, et al. *Pediatric Pain Management and Sedation Handbook*. St Louis: Mosby, 1997:345–374; St Germain Brent A. The management of pain in the emergency department. *Pediatr Clin North Am*. 2000;47:651–679; and Cote CJ, Lerman J, Todres ID, et al. *A Practice of Anesthesia for Infants and Children*. Philadelphia: WB Saunders, 2001.

**BOX 6-3****NALOXONE (NARCAN) ADMINISTRATION**

**INDICATIONS: PATIENTS REQUIRING NALOXONE (NARCAN) USUALLY MEET ALL OF THE FOLLOWING CRITERIA\***

- Unresponsive to physical stimulation
- Shallow respirations or respiratory rate <8 breaths/min<sup>†</sup>
- Pinpoint pupils

**PROCEDURE**

1. **Stop opioid administration** (as well as other sedative drugs), start the **ABCs** (Airway, Breathing, Circulation), and call for **HELP**.
2. **Dilute naloxone:** Mix 0.4 mg (1 ampule) of naloxone with 9 mL of normal saline (final concentration 0.04 mg/mL = 40 mcg/mL)
3. (If child < 40 kg, dilute 0.1 mg (one-fourth ampule) in 9 mL of normal saline to make 0.01 mg/mL solution = 10 mcg/mL)
4. **Administer and observe response:** Administer dilute naloxone *slowly* (1–2 mcg/kg/dose IV over 2 min). Observe patient response.
5. **Titrate to effect:** Within 1–2 min, patient should open eyes and respond. If not, continue until a total dose of 10 mcg/kg is given. If no response is obtained, evaluate for other cause of sedation/respiratory depression.
6. **Discontinue naloxone administration:** Discontinue naloxone as soon as patient responds (e.g., takes deep breaths when directed).
7. **Caution:** Another dose of naloxone may be required within 30 min of first dose (duration of action of naloxone is shorter than that of most opioids).
8. **Monitor patient:** Assign a staff member to monitor sedation/respiratory status and remind patient to take deep breaths as necessary.
9. **Alternative analgesia:** Provide nonopioids for pain relief. Resume opioid administration at half the original dose when the patient is easily aroused and respiratory rate is >9 breaths/min.

\*Patients with significant opiate exposure (sickle cell, cancer) should be carefully evaluated for the need for naloxone. Reversal of analgesia could produce hypertension, tachycardia, ventricular arrhythmias, and pulmonary edema. If necessary, give at the lowest dose possible and titrate carefully.

<sup>†</sup>Respiratory rates that require naloxone vary according to infant's/child's usual rate.

Modified from McCaffery M, Pasero C. *Pain: Clinical Manual*. St Louis: Mosby, 1999:269-270.

3. **Ability to talk and sit up unaided** (if age appropriate).
4. **Alternatively, for very young or intellectually disabled children**, goal is to return as close as possible to presedation level of responsiveness.
5. **Adequate hydration.**
6. **Recovery after sedation protocols** varies but typically ranges from 60–120 minutes.

## **F. Examples of Sedation Protocols (Tables 6-10 and 6-11)**

TABLE 6-10

## EXAMPLES OF SEDATION PROTOCOLS\*

Protocol/Doses	Comments
Ketamine (1 mg/kg/dose IV $\times$ 1–3 doses)	Lowest rates of adverse events when ketamine used alone <sup>‡</sup>
Ketamine + midazolam + atropine (“ketazolam”)	Atropine = antisialagogue
<b>IV route:</b>	Midazolam = counter emergence delirium
Ketamine 1 mg/kg/dose $\times$ 1–3 doses	
Midazolam 0.05 mg/kg $\times$ 1 dose	
Atropine 0.02 mg/kg $\times$ 1 dose	
<b>IM route:</b> combine (use smallest volume possible)	
Ketamine 1.5–2 mg/kg	
Midazolam 0.15–0.2 mg/kg	
Atropine 0.02 mg/kg	
Midazolam + fentanyl	High likelihood of respiratory depression
Midazolam 0.1 mg/kg IV $\times$ 3 doses PRN	Infuse fentanyl no more frequently than Q3 min
Fentanyl 1 mcg/kg IV $\times$ 3 doses PRN	

\*These examples reflect commonly used current protocols at the Johns Hopkins Children's Center; variations are found at other institutions.

<sup>‡</sup>Green, SM, Roback MG, Krauss B, et al. Predictors of emesis and recovery agitation with emergency department ketamine sedation: an individual-patient data meta-analysis of 8,282 children. *Ann Emerg Med.* 2009;54:171-180.

Modified from Yaster M, Cote C, Krane E, et al. *Pediatric Pain Management and Sedation Handbook*. St Louis: Mosby, 1997.

TABLE 6-11

## SUGGESTED ANALGESIA AND SEDATION PROTOCOLS

Pain Threshold	Procedure	Suggested Choices
Nonpainful	CT/MRI/EEG/ECHO	Midazolam*
Mild	Phlebotomy/IV	EMLA
	LP	EMLA ( $\pm$ midazolam)
	Pelvic exam	Midazolam
	Minor laceration, well vascularized	LET
	Minor laceration, not well vascularized	Lidocaine
Moderate	BM aspiration	EMLA ( $\pm$ midazolam)
	Arthrocentesis	Lidocaine (local) for cooperative child or ketamine <sup>†</sup> for uncooperative child
	Fracture reduction	Ketamine
	Major laceration	Ketamine or fentanyl + midazolam
	Burn debridement	Ketamine or fentanyl + midazolam
	Long procedures (>30 min)	Consider general anesthesia
Severe	Fracture reduction	Ketamine
	Long procedures (>30 min)	Consider general anesthesia

\*Caution for antiepileptics for EEG.

<sup>†</sup>Ketamine should not be chosen with head injury or open globe eye injury.

BM, Bone marrow; CT, computed tomography; ECHO, echocardiogram; EEG, electroencephalogram; EMLA, eutectic mixture of local anesthetics; LP, lumbar puncture; LET, lidocaine, epinephrine, tetracaine; MRI, magnetic resonance imaging.

Modified from Yaster M, Cote C, Krane E, et al. *Pediatric Pain Management and Sedation Handbook*. St Louis: Mosby, 1997:551-552.

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# Chapter 7

## Cardiology

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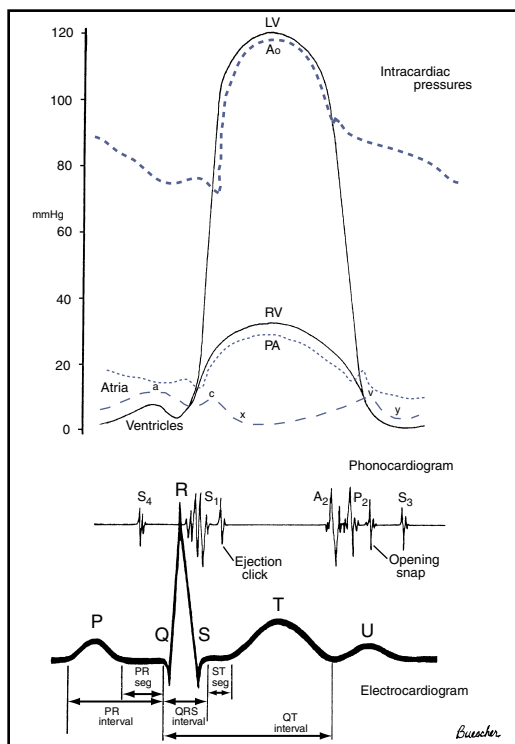
See additional content on Expert Consult

### I. WEBSITES

<http://www.pted.org>

<http://www.murmurlab.org>

### II. THE CARDIAC CYCLE (FIG. 7-1)



**FIGURE 7-1**

The cardiac cycle.

**III. PHYSICAL EXAMINATION****A. Heart Rate**

Refer to [Table 7-4](#) for normal heart rate (HR) by age.

**B. Blood Pressure****1. Blood pressure:**

- a. Blood pressure norms (systolic blood pressure [SBP], diastolic blood pressure [DBP]) by age<sup>1,2</sup>: [Tables 7-1 and 7-2](#); [Figs. 7-2, 7-3, and 7-4](#)  
For blood pressure norms for preterm infants, see Expert Consult: [Table EC 7-A](#).

**2. Pulse pressure** = systolic pressure – diastolic pressure.

- a. Wide pulse pressure (>40 mmHg): Differential diagnosis includes aortic insufficiency, arteriovenous fistula, patent ductus arteriosus, thyrotoxicosis, warm shock.
- b. Narrow pulse pressure (<25 mmHg): Differential diagnosis includes aortic stenosis, pericardial effusion, pericardial tamponade, pericarditis, significant tachycardia, cold shock.

**3. Mean arterial pressure (MAP)**

- a.  $\text{MAP} = \text{diastolic pressure} + (\text{pulse pressure}/3)$  OR  $1/3$  systolic pressure +  $2/3$  diastolic pressure.
- b. Preterm infants and newborns: Normal MAP = gestational age in weeks + 5.

**4. Abnormalities in blood pressure**

- a. Four-limb blood pressure measurements can be used to assess for coarctation of the aorta; pressure must be measured in both the right and left arms because of the possibility of an aberrant right subclavian artery.
- b. Pulsus paradoxus: Exaggeration of the normal drop in SBP seen with inspiration. Determine SBP at the end of exhalation and then during inhalation; if the difference is > 10 mmHg, consider pericardial effusion, tamponade, pericarditis, severe asthma, or restrictive cardiomyopathies.

**C. Heart Sounds**

1. **S<sub>1</sub>**: Associated with closure of mitral and tricuspid valves; heard best at the apex or left lower sternal border (LLSB).
2. **S<sub>2</sub>**: Associated with closure of pulmonary and aortic valves; heard best at the left upper sternal border (LUSB) and has normal physiologic splitting that increases with inspiration.
3. **S<sub>3</sub>**: Heard best at the apex or LLSB.
4. **S<sub>4</sub>**: Heard at the apex.

**D. Systolic and Diastolic Sounds**

See [Box 7-1](#) for abnormal heart sounds.<sup>3</sup>

**E. Murmurs<sup>4</sup>**

More information at <http://www.murmurlab.org>. Clinical characteristics summarized in [Table 7-3](#).<sup>3</sup>

TABLE EC7-A

**BLOOD PRESSURES AFTER 2 WEEKS OF AGE IN INFANTS FROM 26–44 WEEKS POSTCONCEPTIONAL AGE**

Postconceptional Age	50th Percentile	95th Percentile	99th Percentile
<b>44 WEEKS</b>			
SBP	88	105	110
DBP	50	68	73
MAP	63	80	85
<b>42 WEEKS</b>			
SBP	85	98	102
DBP	50	65	70
MAP	62	76	81
<b>40 WEEKS</b>			
SBP	80	95	100
DBP	50	65	70
MAP	60	75	80
<b>38 WEEKS</b>			
SBP	77	92	97
DBP	50	65	70
MAP	59	74	79
<b>36 WEEKS</b>			
SBP	72	87	92
DBP	50	65	70
MAP	57	72	71
<b>34 WEEKS</b>			
SBP	70	85	90
DBP	40	55	60
MAP	50	65	70
<b>32 WEEKS</b>			
SBP	68	83	88
DBP	40	55	60
MAP	48	62	69
<b>30 WEEKS</b>			
SBP	65	80	85
DBP	40	55	60
MAP	48	65	68
<b>28 WEEKS</b>			
SBP	60	75	80
DBP	38	50	54
MAP	45	58	63
<b>26 WEEKS</b>			
SBP	55	72	77
DBP	30	50	56
MAP	38	57	63

DBP, Diastolic blood pressure; MAP, mean arterial pressure; SBP, systolic blood pressure.

Data from Dionne J et al. Hypertension in infancy: diagnosis, management, and outcome. *Pediatr Nephrol*. 2012;27:17-32.

TABLE 7-1

BLOOD PRESSURE LEVELS FOR THE 50TH, 90TH, 95TH, AND 99TH PERCENTILES OF BLOOD PRESSURE FOR GIRLS AGE 1–17 YEARS BY PERCENTILES OF HEIGHT<sup>2</sup>

Age, yr	BP Percentile <sup>†</sup>	SBP, mmHg							DBP, mmHg						
		Percentile of Height <sup>*</sup>							Percentile of Height <sup>*</sup>						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	50th	83	84	85	86	88	89	90	38	39	39	40	41	41	42
	90th	97	97	98	100	101	102	103	52	53	53	54	55	55	56
	95th	100	101	102	104	105	106	107	56	57	57	58	59	59	60
	99th	108	108	109	111	112	113	114	64	64	65	65	66	67	67
2	50th	85	85	87	88	89	91	91	43	44	44	45	46	46	47
	90th	98	99	100	101	103	104	105	57	58	58	59	60	61	61
	95th	102	103	104	105	107	108	109	61	62	62	63	64	65	65
	99th	109	110	111	112	114	115	116	69	69	70	70	71	72	72
3	50th	86	87	88	89	91	92	93	47	48	48	49	50	50	51
	90th	100	100	102	103	104	106	106	61	62	62	63	64	64	65
	95th	104	104	105	107	108	109	110	65	66	66	67	68	68	69
	99th	111	111	113	114	115	116	117	73	73	74	74	75	76	76
4	50th	88	88	90	91	92	94	94	50	50	51	52	52	53	54
	90th	101	102	103	104	106	107	108	64	64	65	66	67	67	68
	95th	105	106	107	108	110	111	112	68	68	69	70	71	71	72
	99th	112	113	114	115	117	118	119	76	76	76	77	78	79	79
5	50th	89	90	91	93	94	95	96	52	53	53	54	55	55	56
	90th	103	103	105	106	107	109	109	66	67	67	68	69	69	70
	95th	107	107	108	110	111	112	113	70	71	71	72	73	73	74
	99th	114	114	116	117	118	120	120	78	78	79	79	80	81	81

Continued



TABLE 7-1

**BLOOD PRESSURE LEVELS FOR THE 50TH, 90TH, 95TH, AND 99TH PERCENTILES OF BLOOD PRESSURE FOR GIRLS AGE 1–17 YEARS BY PERCENTILES OF HEIGHT (Continued)**

Age, yr	BP Percentil	SBP, mmHg							DBP, mmHg						
		Percentile of Height*							Percentile of Height*						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
6	50th	91	92	93	94	96	97	98	54	54	55	56	56	57	58
	90th	104	105	106	108	109	110	111	68	68	69	70	70	71	72
	95th	108	109	110	111	113	114	115	72	72	73	74	74	75	76
	99th	115	116	117	119	120	121	122	80	80	80	81	82	83	83
7	50th	93	93	95	96	97	99	99	55	56	56	57	58	58	59
	90th	106	107	108	109	111	112	113	69	70	70	71	72	72	73
	95th	110	111	112	113	115	116	116	73	74	74	75	76	76	77
	99th	117	118	119	120	122	123	124	81	81	82	82	83	84	84
8	50th	95	95	96	98	99	100	101	57	57	57	58	59	60	60
	90th	108	109	110	111	113	114	114	71	71	71	72	73	74	74
	95th	112	112	114	115	116	118	118	75	75	75	76	77	78	78
	99th	119	120	121	122	123	125	125	82	82	83	83	84	85	86
9	50th	96	97	98	100	101	102	103	58	58	58	59	60	61	61
	90th	110	110	112	113	114	116	116	72	72	72	73	74	75	75
	95th	114	114	115	117	118	119	120	76	76	76	77	78	79	79
	99th	121	121	123	124	125	127	127	83	83	84	84	85	86	87
10	50th	98	99	100	102	103	104	105	59	59	59	60	61	62	62
	90th	112	112	114	115	116	118	118	73	73	73	74	75	76	76
	95th	116	116	117	119	120	121	122	77	77	77	78	79	80	80

TABLE 7-1

**BLOOD PRESSURE LEVELS FOR THE 50TH, 90TH, 95TH, AND 99TH PERCENTILES OF BLOOD PRESSURE FOR GIRLS AGE 1–17 YEARS BY PERCENTILES OF HEIGHT (Continued)**

Age, yr	BP Percentile <sup>†</sup>	SBP, mmHg							DBP, mmHg						
		Percentile of Height <sup>*</sup>							Percentile of Height <sup>*</sup>						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
11	99th	123	123	125	126	127	129	129	84	84	85	86	86	87	88
	50th	100	101	102	103	105	106	107	60	60	60	61	62	63	63
	90th	114	114	116	117	118	119	120	74	74	74	75	76	77	77
12	95th	118	118	119	121	122	123	124	78	78	78	79	80	81	81
	99th	125	125	126	128	129	130	131	85	85	86	87	87	88	89
	50th	102	103	104	105	107	108	109	61	61	61	62	63	64	64
13	90th	116	116	117	119	120	121	122	75	75	75	76	77	78	78
	95th	119	120	121	123	124	125	126	79	79	79	80	81	82	82
	99th	127	127	128	130	131	132	133	86	86	87	88	88	89	90
14	50th	104	105	106	107	109	110	110	62	62	62	63	64	65	65
	90th	117	118	119	121	122	123	124	76	76	76	77	78	79	79
	95th	121	122	123	124	126	127	128	80	80	80	81	82	83	83
15	99th	128	129	130	132	133	134	135	87	87	88	89	89	90	91
	50th	106	106	107	109	110	111	112	63	63	63	64	65	66	66
	90th	119	120	121	122	124	125	125	77	77	77	78	79	80	80
16	95th	123	123	125	126	127	129	129	81	81	81	82	83	84	84
	99th	130	131	132	133	135	136	136	88	88	89	90	90	91	92
	50th	107	108	109	110	111	113	113	64	64	64	65	66	67	67
17	90th	120	121	122	123	125	126	127	78	78	78	79	80	81	81
	95th	124	125	126	127	129	130	131	82	82	82	83	84	85	85

Continued

TABLE 7-1

**BLOOD PRESSURE LEVELS FOR THE 50TH, 90TH, 95TH, AND 99TH PERCENTILES OF BLOOD PRESSURE FOR GIRLS AGE 1–17 YEARS BY PERCENTILES OF HEIGHT (Continued)**

Age, yr	BP Percentile <sup>†</sup>	SBP, mmHg							DBP, mmHg						
		Percentile of Height <sup>*</sup>							Percentile of Height <sup>*</sup>						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
16	99th	131	132	133	134	136	137	138	89	89	90	91	91	92	93
	50th	108	108	110	111	112	114	114	64	64	65	66	66	67	68
	90th	121	122	123	124	126	127	128	78	78	79	80	81	81	82
	95th	125	126	127	128	130	131	132	82	82	83	84	85	85	86
17	99th	132	133	134	135	137	138	139	90	90	90	91	92	93	93
	50th	108	109	110	111	113	114	115	64	65	65	66	67	67	68
	90th	122	122	123	125	126	127	128	78	79	79	80	81	81	82
	95th	125	126	127	129	130	131	132	82	83	83	84	85	85	86
	99th	133	133	134	136	137	138	139	90	90	91	91	92	93	93

\*Height percentile determined by standard growth curves.

<sup>†</sup>Blood pressure percentile determined by a single measurement.

Adapted from National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. *Pediatrics*. 2004;114(2 Suppl):555-576.

TABLE 7-2

BLOOD PRESSURE LEVELS FOR THE 50TH, 90TH, 95TH, AND 99TH PERCENTILES OF BLOOD PRESSURE FOR BOYS AGE 1–17 YEARS BY PERCENTILES OF HEIGHT<sup>2</sup>

Age, yr	BP Percentile <sup>†</sup>	SBP, mmHg							DBP, mmHg						
		Percentile of Height*							Percentile of Height*						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	50th	80	81	83	85	87	88	89	34	35	36	37	38	39	39
	90th	94	95	97	99	100	102	103	49	50	51	52	53	53	54
	95th	98	99	101	103	104	106	106	54	54	55	56	57	58	58
	99th	105	106	108	110	112	113	114	61	62	63	64	65	66	66
2	50th	84	85	87	88	90	92	92	39	40	41	42	43	44	44
	90th	97	99	100	102	104	105	106	54	55	56	57	58	58	59
	95th	101	102	104	106	108	109	110	59	59	60	61	62	63	63
	99th	109	110	111	113	115	117	117	66	67	68	69	70	71	71
3	50th	86	87	89	91	93	94	95	44	44	45	46	47	48	48
	90th	100	101	103	105	107	108	109	59	59	60	61	62	63	63
	95th	104	105	107	109	110	112	113	63	63	64	65	66	67	67
	99th	111	112	114	116	118	119	120	71	71	72	73	74	75	75
4	50th	88	89	91	93	95	96	97	47	48	49	50	51	51	52
	90th	102	103	105	107	109	110	111	62	63	64	65	66	66	67
	95th	106	107	109	111	112	114	115	66	67	68	69	70	71	71
	99th	113	114	116	118	120	121	122	74	75	76	77	78	78	79
5	50th	90	91	93	95	96	98	98	50	51	52	53	54	55	55
	90th	104	105	106	108	110	111	112	65	66	67	68	69	69	70
	95th	108	109	110	112	114	115	116	69	70	71	72	73	74	74
	99th	115	116	118	120	121	123	123	77	78	79	80	81	81	82
6	50th	91	92	94	96	98	99	100	53	53	54	55	56	57	57
	90th	105	106	108	110	111	113	113	68	68	69	70	71	72	72
	95th	109	110	112	114	115	117	117	72	72	73	74	75	76	76
	99th	116	117	119	121	123	124	125	80	80	81	82	83	84	84

TABLE 7-2

**BLOOD PRESSURE LEVELS FOR THE 50TH, 90TH, 95TH, AND 99TH PERCENTILES OF BLOOD PRESSURE FOR BOYS AGE 1–17 YEARS BY PERCENTILES OF HEIGHT (Continued)**

Age, yr	BP Percentile†	SBP, mmHg							DBP, mmHg						
		Percentile of Height*							Percentile of Height*						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
7	50th	92	94	95	97	99	100	101	55	55	56	57	58	59	59
	90th	106	107	109	111	113	114	115	70	70	71	72	73	74	74
	95th	110	111	113	115	117	118	119	74	74	75	76	77	78	78
	99th	117	118	120	122	124	125	126	82	82	83	84	85	86	86
8	50th	94	95	97	99	100	102	102	56	57	58	59	60	60	61
	90th	107	109	110	112	114	115	116	71	72	72	73	74	75	76
	95th	111	112	114	116	118	119	120	75	76	77	78	79	79	80
	99th	119	120	122	123	125	127	127	83	84	85	86	87	87	88
9	50th	95	96	98	100	102	103	104	57	58	59	60	61	61	62
	90th	109	110	112	114	115	117	118	72	73	74	75	76	76	77
	95th	113	114	116	118	119	121	121	76	77	78	79	80	81	81
	99th	120	121	123	125	127	128	129	84	85	86	87	88	88	89
10	50th	97	98	100	102	103	105	106	58	59	60	61	61	62	63
	90th	111	112	114	115	117	119	119	73	73	74	75	76	77	78
	95th	115	116	117	119	121	122	123	77	78	79	80	81	81	82
	99th	122	123	125	127	128	130	130	85	86	86	88	88	89	90
11	50th	99	100	102	104	105	107	107	59	59	60	61	62	63	63
	90th	113	114	115	117	119	120	121	74	74	75	76	77	78	78
	95th	117	118	119	121	123	124	125	78	78	79	80	81	82	82
	99th	124	125	127	129	130	132	132	86	86	87	88	89	90	90
12	50th	101	102	104	106	108	109	110	59	60	61	62	63	63	64
	90th	115	116	118	120	121	123	123	74	75	75	76	77	78	79
	95th	119	120	122	123	125	127	127	78	79	80	81	82	82	83
	99th	126	127	129	131	133	134	135	86	87	88	89	90	90	91

TABLE 7-2

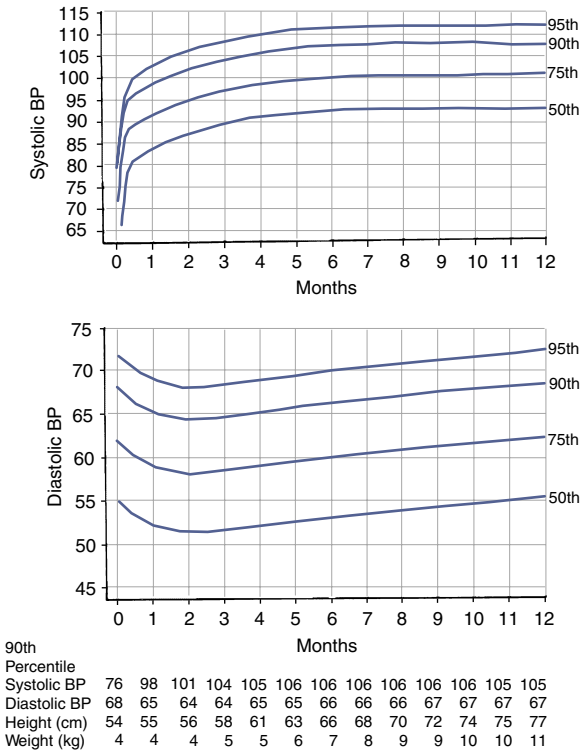
# BLOOD PRESSURE LEVELS FOR THE 50TH, 90TH, 95TH, AND 99TH PERCENTILES OF BLOOD PRESSURE FOR BOYS AGE 1–17 YEARS BY PERCENTILES OF HEIGHT (Continued)

Age, yr	BP Percentile <sup>†</sup>	SBP, mmHg							DBP, mmHg						
		Percentile of Height*							Percentile of Height*						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
13	50th	104	105	106	108	110	111	112	60	60	61	62	63	64	64
	90th	117	118	120	122	124	125	126	75	75	76	77	78	79	79
	95th	121	122	124	126	128	129	130	79	79	80	81	82	83	83
	99th	128	130	131	133	135	136	137	87	87	88	89	90	91	91
14	50th	106	107	109	111	113	114	115	60	61	62	63	64	65	65
	90th	120	121	123	125	126	128	128	75	76	77	78	79	79	80
	95th	124	125	127	128	130	132	132	80	80	81	82	83	84	84
	99th	131	132	134	136	138	139	140	87	88	89	90	91	92	92
15	50th	109	110	112	113	115	117	117	61	62	63	64	65	66	66
	90th	122	124	125	127	129	130	131	76	77	78	79	80	80	81
	95th	126	127	129	131	133	134	135	81	81	82	83	84	85	85
	99th	134	135	136	138	140	142	142	88	89	90	91	92	93	93
16	50th	111	112	114	116	118	119	120	63	63	64	65	66	67	67
	90th	125	126	128	130	131	133	134	78	78	79	80	81	82	82
	95th	129	130	132	134	135	137	137	82	83	83	84	85	86	87
	99th	136	137	139	141	143	144	145	90	90	91	92	93	94	94
17	50th	114	115	116	118	120	121	122	65	66	66	67	68	69	70
	90th	127	128	130	132	134	135	136	80	80	81	82	83	84	84
	95th	131	132	134	136	138	139	140	84	85	86	87	87	88	89
	99th	139	140	141	143	145	146	147	92	93	93	94	95	96	97

\*Height percentile determined by standard growth curves.

<sup>†</sup>Blood pressure percentile determined by a single measurement.

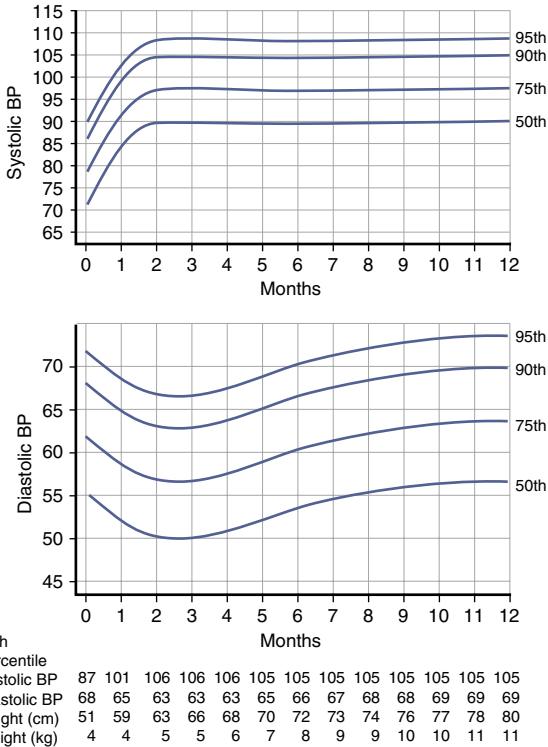
Adapted from National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents: The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. *Pediatrics* 2004;114(2 Suppl):555–576.



**FIGURE 7-2**

Age-specific percentiles of blood pressure (BP) measurements in boys from birth to 12 months of age; Korotkoff phase IV (K4) used for diastolic BP. (*From Task Force on Blood Pressure Control in Children. Report of the Second Task Force on Blood Pressure Control in Children. Pediatrics. 1987;79:1-25.*)

1. **Grading of heart murmurs:** Intensified by states of higher cardiac output (e.g., anemia, anxiety, fever, exercise)<sup>3</sup>
  - a. Grade I: Barely audible
  - b. Grade II: Soft but easily audible
  - c. Grade III: Moderately loud but not accompanied by a thrill
  - d. Grade IV: Louder, associated with a thrill
  - e. Grade V: Audible with a stethoscope barely on the chest
  - f. Grade VI: Audible with a stethoscope off the chest

**FIGURE 7-3**

Age-specific percentile of blood pressure (BP) measurements in girls from birth to 12 months of age; Korotkoff phase IV (K4) used for diastolic BP. (From Task Force on Blood Pressure Control in Children. Report of the Second Task Force on Blood Pressure Control in Children. Pediatrics. 1987;79:1-25.)

## 2. Benign heart murmurs:

- Caused by a disturbance of the laminar flow of blood; frequently produced as the diameter of the blood's pathway decreases and velocity increases.
- Present in > 80% of children sometime during childhood, most commonly beginning at age 3 to 4 years.
- Accentuated in high-output states, especially with fever and anemia.
- Normal electrocardiogram (ECG) and radiographic findings.

**NOTE:** ECG and chest radiograph are not routinely useful or cost-effective screening tools for distinguishing benign from pathologic murmurs.



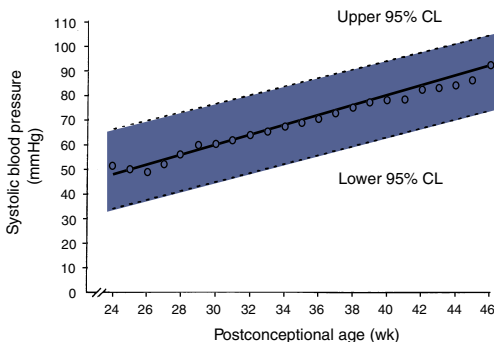


FIGURE 7-4

Linear regression of mean systolic blood pressure on postconceptional age (gestational age in weeks plus weeks after delivery). CL, Confidence limit. (Data from Zubrow AB, Hulman S, Kushner H, et al. Determinants of blood pressure in infants admitted to neonatal intensive care units: a prospective multicenter study. Philadelphia Neonatal Blood Pressure Study Group. *J Perinatol.* 1995;15:470-479.)

## BOX 7-1

## SUMMARY OF ABNORMAL HEART SOUNDS

- **Widely split S<sub>1</sub>:** Ebstein anomaly, RBBB
- **Widely split and fixed S<sub>2</sub>:** Right ventricular volume overload (e.g., ASD, PAPVR), pressure overload (e.g., PS), electrical delay in RV contraction (e.g., RBBB), early aortic closure (e.g., MR), occasionally heard in normal child
- **Narrowly split S<sub>2</sub>:** Pulmonary hypertension, AS, delay in LV contraction (e.g., LBBB), occasionally heard in normal child
- **Single S<sub>2</sub>:** Pulmonary hypertension, one semilunar valve (e.g., pulmonary atresia, aortic atresia, truncus arteriosus), P2 not audible (e.g., TGA, TOF, severe PS), severe AS, occasionally heard in normal child
- **Paradoxically split S<sub>2</sub>:** Severe AS, LBBB, Wolff-Parkinson-White syndrome (type B)
- **Abnormal intensity of P2:** Increased P2 (e.g., pulmonary hypertension), decreased P2 (e.g., severe PS, TOF, TS)
- **S<sub>3</sub>:** Occasionally heard in healthy children or adults or may indicate dilated ventricles (e.g., large VSD, CHF)
- **S<sub>4</sub>:** Always pathologic; decreased ventricular compliance
- **Ejection click:** Heard with stenosis of the semilunar valves, dilated great arteries in the setting of pulmonary or systemic hypertension, idiopathic dilation of the PA, TOF, persistent truncus arteriosus
- **Midsystolic click:** Heard at the apex in mitral valve prolapse
- **Diastolic opening snap:** Rare in children; associated with TS/MS

AS, Aortic stenosis; ASD, atrial septal defect; CHF, congestive heart failure; LBBB, left bundle-branch block; MR, mitral regurgitation; MS, mitral stenosis; PA, pulmonary artery; PAPVR, partial anomalous pulmonary venous return; PS, pulmonary stenosis; RBBB, right bundle-branch block; RV, right ventricular; TGA, transposition of the great arteries; TOF, tetralogy of Fallot; TS, tricuspid stenosis; VSD, ventricular septal defect.

Modified from Park MK. *Pediatric Cardiology for Practitioners*. 5th ed. St Louis: Mosby; 2008:25.

3. **Likely pathologic murmur** when one or more of the following are present: Symptoms; cyanosis; systolic murmur that is loud (grade  $\geq 3/6$ ), harsh, pansystolic, or long in duration; diastolic murmur; abnormal heart sounds; presence of a click; abnormally strong or weak pulses.
4. **Systolic and diastolic heart murmurs** (Box 7-2)

TABLE 7-3

**COMMON INNOCENT HEART MURMURS**

Type (Timing)	Description of Murmur	Age Group
Classic vibratory murmur (Still's murmur; systolic)	Maximal at LMSB or between LLSB and apex Grade 2–3/6 in intensity Low-frequency vibratory, twanging string, groaning, squeaking, or musical	3–6 yr; occasionally in infancy
Pulmonary ejection murmur (systolic)	Maximal at LUSB Early to midsystolic Grade 1–3/6 in intensity Blowing in quality	8–14 yr
Pulmonary flow murmur of newborn (systolic)	Maximal at LUSB Transmits well to left and right chest, axilla, and back Grade 1–2/6 in intensity	Premature and full-term newborns Usually disappears by 3–6 mo
Venous hum (continuous)	Maximal at right (or left) supraclavicular and infraclavicular areas Grade 1–3/6 in intensity Inaudible in supine position Intensity changes with rotation of head and disappears with compression of jugular vein.	3–6 yr
Carotid bruit (systolic)	Right supraclavicular area over carotids Grade 2–3/6 in intensity Occasional thrill over carotid	Any age

LLSB, Left lower sternal border; LMSB, left middle sternal border; LUSB, left upper sternal border.

From Park MK. *Pediatric Cardiology for Practitioners*. 5th ed. St Louis: Mosby; 2008:36.

**BOX 7-2****SYSTOLIC AND DIASTOLIC HEART MURMURS****I. RUSB**

Aortic valve stenosis (supraaortic, subaortic)

*Aortic regurgitation*

**II. LUSB**

Pulmonary valve stenosis

Atrial septal defect

Pulmonary ejection murmur, innocent

Pulmonary flow murmur of newborn

Pulmonary artery stenosis

Aortic stenosis

Coarctation of the aorta

Patent ductus arteriosus

*Continued*

**BOX 7-2****SYSTOLIC AND DIASTOLIC HEART MURMURS (Continued)**

Partial anomalous pulmonary venous return (PAPVR)

Total anomalous pulmonary venous return (TAPVR)

*Pulmonary regurgitation*

**III. LLSB**

Ventricular septal defect, including atrioventricular septal defect

Vibratory innocent murmur (Still's murmur)

HOCM (IHSS)

Tricuspid regurgitation

Tetralogy of Fallot

*Tricuspid stenosis*

**IV. APEX**

Mitral regurgitation

Vibratory innocent murmur (Still's murmur)

Mitral valve prolapse

Aortic stenosis

HOCM (IHSS)

*Mitral stenosis*

The location at which various murmurs may be heard. *Diastolic murmurs are in italics.* HOCM, Hypertrophic obstructive cardiomyopathy; IHSS, idiopathic hypertrophic subaortic stenosis; LLSB, left lower sternal border; LUSB, left upper sternal border; RUSB, right upper sternal border.

From Park MK. *Pediatric Cardiology for Practitioners*. 5th ed. St Louis: Mosby; 2008:30.

**IV. ELECTROCARDIOGRAPHY****A. Basic Electrocardiography Principles**

1. **Lead placement** (Fig. 7-5)
2. **ECG complexes** (see Fig. 7-1)
  - a. P wave: Represents atrial depolarization
  - b. QRS complex: Represents ventricular depolarization
  - c. T wave: Represents ventricular repolarization
  - d. U wave: May follow T wave, representing late phases of ventricular repolarization
3. **Systematic approach for evaluating ECGs** (Table 7-4 shows normal ECG parameters)<sup>3,5</sup>:
  - a. Rate
    - (1) Standardization: Paper speed is 25 mm/sec. One small square = 1 mm = 0.04 sec. One large square = 5 mm = 0.2 sec. Amplitude standard: 10 mm = 1 mV
    - (2) Calculation: HR (beats per minute) = 60 divided by the average R-R interval in seconds, or 1500 divided by the R-R interval in millimeters
  - b. Rhythm
    - (1) Sinus rhythm: Every QRS complex is preceded by a P wave, normal PR interval (although PR interval may be prolonged, as in first-degree atrioventricular [AV] block), and normal P-wave axis (upright P in lead I and aVF).

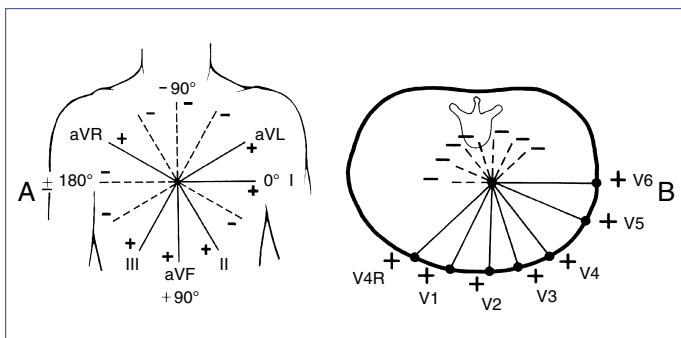


FIGURE 7-5

**A**, Hexaxial reference system. **B**, Horizontal reference system. (Modified from Park MK, Guntheroth WG. *How to Read Pediatric ECGs*. 4th ed. Philadelphia: Mosby; 2006:3.)

- (2) There is normal respiratory variation of the R-R interval without morphologic changes of the P wave or QRS complex.
- c. Axis: Look at the direction of the QRS in leads I and aVF. Determine quadrant and compare with age-matched normal values (Fig. 7-6; see Table 7-4).
- d. Intervals (PR, QRS, QTc): See Table 7-4 for normal PR and QRS intervals. The QTc is calculated using the Bazett formula:

$$QTc = QT \text{ (sec) measured} / \sqrt{R-R}$$

(average 3 measurements taken from same lead)

R-R interval should extend from the R wave in the QRS complex where you are measuring QT to the preceding R wave. Normal values for QTc are:

- (1) 0.44 sec is 97th percentile for infants 3–4 days old<sup>6</sup>
- (2)  $\leq 0.45$  sec in all males  $>1$  week of age and prepubescent females
- (3)  $\leq 0.46$  sec for postpubescent females
- e. P-wave size and shape: Normal P wave should be  $<0.10$  sec in children,  $<0.08$  sec in infants, with amplitude  $<0.3$  mV (3 mm in height, with normal standardization)
- f. R-wave progression: Generally a normal increase in R-wave size and decrease in S-wave size from leads  $V_1$  to  $V_6$  (with dominant S waves in right precordial leads and dominant R waves in left precordial leads), representing dominance of left ventricular forces. However, newborns and infants have a normal dominance of the right ventricle.
- g. Q waves: Normal Q waves usually  $<0.04$  sec in duration and  $<25\%$  of total QRS amplitude. Q waves are  $<5$  mm deep in left precordial leads and aVF and  $\leq 8$  mm deep in lead III for children  $<3$  years of age.

TABLE 7-4

## NORMAL PEDIATRIC ELECTROCARDIOGRAM (ECG) PARAMETERS

Age	Heart Rate (bpm)	QRS Axis*	PR Interval (sec)*	QRS Duration (sec)†	Lead V <sub>1</sub>			Lead V <sub>6</sub>		
					R-Wave Amplitude (mm)†	S-Wave Amplitude (mm)†	R/S Ratio	R-Wave Amplitude (mm)†	S-Wave Amplitude (mm)†	R/S Ratio
0–7 days	95–160 (125)	+30 to 180 (110)	0.08–0.12 (0.10)	0.05 (0.07)	13.3 (25.5)	7.7 (18.8)	2.5	4.8 (11.8)	3.2 (9.6)	2.2
1–3 wk	105–180 (145)	+30 to 180 (110)	0.08–0.12 (0.10)	0.05 (0.07)	10.6 (20.8)	4.2 (10.8)	2.9	7.6 (16.4)	3.4 (9.8)	3.3
1–6 mo	110–180 (145)	+10 to +125 (+70)	0.08–0.13 (0.11)	0.05 (0.07)	9.7 (19)	5.4 (15)	2.3	12.4 (22)	2.8 (8.3)	5.6
6–12 mo	110–170 (135)	+10 to +125 (+60)	0.10–0.14 (0.12)	0.05 (0.07)	9.4 (20.3)	6.4 (18.1)	1.6	12.6 (22.7)	2.1 (7.2)	7.6
1–3 yr	90–150 (120)	+10 to +125 (+60)	0.10–0.14 (0.12)	0.06 (0.07)	8.5 (18)	9 (21)	1.2	14 (23.3)	1.7 (6)	10
4–5 yr	65–135 (110)	0 to +110 (+60)	0.11–0.15 (0.13)	0.07 (0.08)	7.6 (16)	11 (22.5)	0.8	15.6 (25)	1.4 (4.7)	11.2
6–8 yr	60–130 (100)	–15 to +110 (+60)	0.12–0.16 (0.14)	0.07 (0.08)	6 (13)	12 (24.5)	0.6	16.3 (26)	1.1 (3.9)	13
9–11 yr	60–110 (85)	–15 to +110 (+60)	0.12–0.17 (0.14)	0.07 (0.09)	5.4 (12.1)	11.9 (25.4)	0.5	16.3 (25.4)	1.0 (3.9)	14.3
12–16 yr	60–110 (85)	–15 to +110 (+60)	0.12–0.17 (0.15)	0.07 (0.10)	4.1 (9.9)	10.8 (21.2)	0.5	14.3 (23)	0.8 (3.7)	14.7
>16 yr	60–100 (80)	–15 to +110 (+60)	0.12–0.20 (0.15)	0.08 (0.10)	3 (9)	10 (20)	0.3	10 (20)	0.8 (3.7)	12

\*Normal range and (mean).

†Mean and (98th percentile).

Adapted from Park MK. *Pediatric Cardiology for Practitioners*. 5th ed. St Louis: Mosby; 2008; and Davignon A et al. Normal ECG standards for infants and children. *Pediatr Cardiol*. 1979;1:123-131.

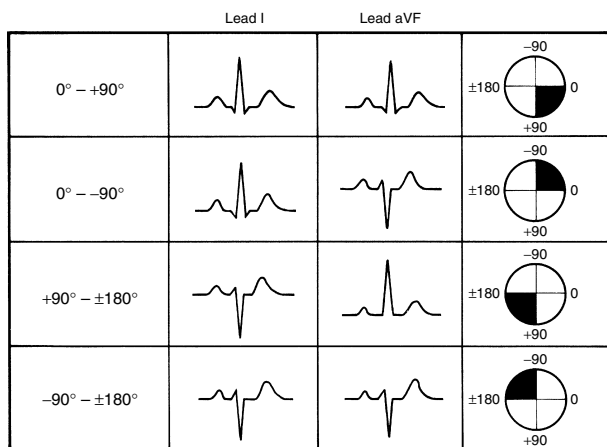


FIGURE 7-6

Locating quadrants of mean QRS axis from leads I and aVF. (From Park MK, Guntheroth WG. How to Read Pediatric ECGs. 4th ed. Philadelphia: Mosby; 2006:17.)

TABLE 7-5

## NORMAL T-WAVE AXIS

Age	$V_1, V_2$	AVF	$I, V_5, V_6$
Birth–1 day	±	+	±
1–4 days	±	+	+
4 days to adolescent	–	+	+
Adolescent to adult	+	+	+

+, T wave positive; –, T wave negative; ±, T wave normally either positive or negative.

- h. ST-segment (Fig. 7-7): ST-segment elevation or depression  $>1$  mm in limb leads and  $>2$  mm in precordial leads is consistent with myocardial ischemia or injury. **Note:** J-depression is an upsloping of the ST segment and a normal variant.
- i. T wave:
  - (1) Inverted T waves in  $V_1$  and  $V_2$  can be normal in children up to adolescence (Table 7-5).
  - (2) Tall, peaked T waves may be seen in hyperkalemia.
  - (3) Flat or low T waves may be seen in hypokalemia, hypothyroidism, normal newborns, and myocardial/pericardial ischemia and inflammation.

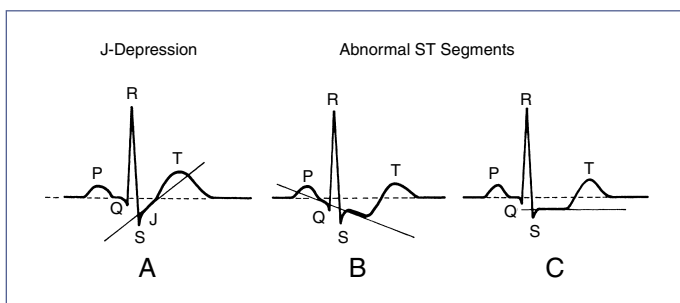


FIGURE 7-7

Nonpathologic (nonischemic) and pathologic (ischemic) ST and T changes. **A**, Characteristic nonischemic ST-segment alteration called *J-depression*; note that ST slope is upward. **B–C**, Ischemic or pathologic ST-segment alterations. **B**, Downward slope of ST segment. **C**, Horizontal segment is sustained. (From Park MK, Guntheroth WG. *How to Read Pediatric ECGs*. 4th ed. Philadelphia: Mosby; 2006:107.)

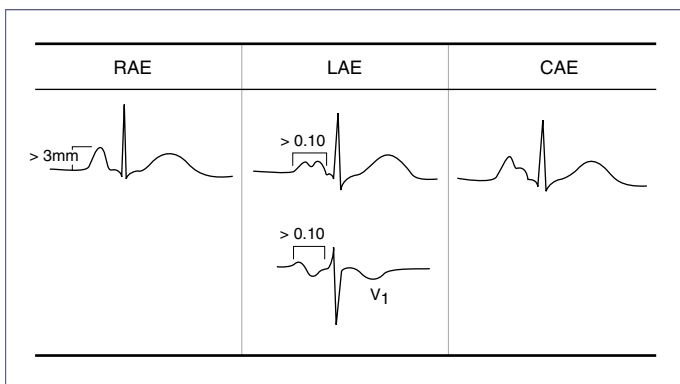


FIGURE 7-8

Criteria for atrial enlargement. CAE, Combined atrial enlargement; LAE, left atrial enlargement; RAE, right atrial enlargement. (From Park MK. *Pediatric Cardiology for Practitioners*. 5th ed. St Louis: Mosby; 2008:53.)

#### j. Hypertrophy/enlargement

(1) Atrial enlargement (Fig. 7-8)

(2) Ventricular hypertrophy: Diagnosed by QRS axis, voltage, and R/S ratio (Box 7-3; see also Table 7-4)

### B. ECG Abnormalities

1. **Nonventricular arrhythmias** (Table 7-6; Figs. 7-9 and 7-10)<sup>7</sup>

2. **Ventricular arrhythmias** (Table 7-7; Fig. 7-11)

3. **Nonventricular conduction disturbances** (Fig. 7-12 and Table 7-8)<sup>8</sup>

4. **Ventricular conduction disturbances** (Table 7-9)

## BOX 7-3

## VENTRICULAR HYPERTROPHY CRITERIA

## RIGHT VENTRICULAR HYPERTROPHY (RVH) CRITERIA

**Must Have at Least One of the Following:**Upright T wave in lead  $V_1$  after 3 days of age to adolescencePresence of Q wave in  $V_1$  (QR or QRS pattern)

Increased right and anterior QRS voltage (with normal QRS duration):

R in lead  $V_1$ , >98th percentile for ageS in lead  $V_6$ , >98th percentile for ageRight ventricular strain (associated with inverted T wave in  $V_1$  with tall R wave)

## LEFT VENTRICULAR HYPERTROPHY (LVH) CRITERIA

Left ventricular strain (associated with inverted T wave in leads  $V_6$ , I, and/or aVF)**Supplemental Criteria:**

Left axis deviation (LAD) for patient's age

Volume overload (associated with Q wave >5mm and tall T waves in  $V_5$  or  $V_6$ )

Increased QRS voltage in left leads (with normal QRS duration):

R in lead  $V_6$  (and I, aVL,  $V_5$ ), >98th percentile for ageS in lead  $V_1$ , >98th percentile for age

TABLE 7-6

## NONVENTRICULAR ARRHYTHMIAS

Name/Description	Cause	Treatment
<b>SINUS</b>		
<b>TACHYCARDIA</b>		
Normal sinus rhythm with HR >95th percentile for age (usually infants: <220 beats/min and children: <180 beats/min)	Hypovolemia, shock, anemia, sepsis, fever, anxiety, CHF, PE, myocardial disease, drugs (e.g., $\beta$ -agonists, albuterol, caffeine, atropine)	Address underlying cause
<b>BRADYCARDIA</b>		
Normal sinus rhythm with HR <5th percentile for age	Normal (especially in athletic individuals), increased ICP, hypoxia, hyperkalemia, hypercalcemia, vagal stimulation, hypothyroidism, hypothermia, drugs (e.g., opioids, digoxin, $\beta$ -blockers), long QT	Address underlying cause; if symptomatic, refer to inside back cover for bradycardia algorithm
<b>SUPRAVENTRICULAR*</b>		
<b>PREMATURE ATRIAL CONTRACTION (PAC)</b>		
Narrow QRS complex; ectopic focus in atria with abnormal P-wave morphology	Digitalis toxicity, medications (e.g., caffeine, theophylline, sympathomimetics), normal variant	Treat digitalis toxicity; otherwise no treatment needed
<b>ATRIAL FLUTTER</b>		
Atrial rate 250–350 beats/min; characteristic sawtooth or flutter pattern with variable ventricular response rate and normal QRS complex	Dilated atria, previous intra-atrial surgery, valvular or ischemic heart disease, idiopathic in newborns	Synchronized cardioversion or overdrive pacing; treat underlying cause

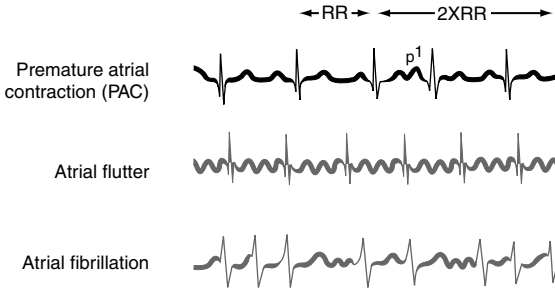


TABLE 7-6

## NONVENTRICULAR ARRHYTHMIAS (Continued)

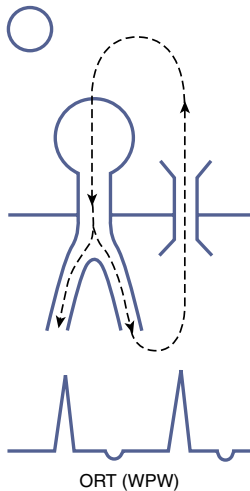
Name/Description	Cause	Treatment
<b>ATRIAL FIBRILLATION</b>		
Irregular; atrial rate 350–600 beats/min, yielding characteristic fibrillatory pattern (no discrete P waves) and irregular ventricular response rate of about 110–150 beats/min with normal QRS complex	Wolff-Parkinson-White syndrome and those listed previously for atrial flutter (except not idiopathic), alcohol exposure, familial	Synchronized cardioversion; then may need anticoagulation pretreatment
<b>SVT</b>		
Sudden run of three or more consecutive premature supraventricular beats at >220 beats/min (infant) or >180 beats/min (child), with narrow QRS complex and absent/abnormal P wave; either sustained (>30 sec) or nonsustained	Most commonly idiopathic but may be seen in congenital heart disease (e.g., Ebstein anomaly, transposition)	Vagal maneuvers, adenosine; if unstable, need immediate synchronized cardioversion (0.5 J/kg up to 1 J/kg). Consult cardiologist. See “Tachycardia with Poor Perfusion” or “Tachycardia with Adequate Perfusion” algorithms in back of handbook.
<i>I. AV Reentrant:</i> Presence of accessory bypass pathway, in conjunction with AV node, establishes cyclic pattern of reentry independent of SA node; most common cause of nonsinus tachycardia in children (see Wolff-Parkinson-White syndrome, Table 7-9 and Fig. 7-10)		
<i>II. Junctional:</i> Automatic focus; simultaneous depolarization of atria and ventricles yields invisible P wave or retrograde P wave	Cardiac surgery, idiopathic	Adjust for clinical situation; consult cardiology
<i>III. Ectopic atrial tachycardia:</i> Rapid firing of ectopic focus in atrium	Idiopathic	AV nodal blockade, ablation
<b>NODAL ESCAPE/JUNCTIONAL RHYTHM</b>		
Abnormal rhythm driven by AV node impulse, giving normal QRS complex and invisible P wave (buried in preceding QRS or T wave) or retrograde P wave (negative in lead II, positive in aVR); seen in sinus bradycardia	Common after surgery of atria	Often requires no treatment. If rate is slow enough, may require pacemaker.

\*Abnormal rhythm resulting from ectopic focus in atria or AV node, or from accessory conduction pathways. Characterized by different P-wave shape and abnormal P-wave axis. QRS morphology usually normal. See Figures 7-9, 7-10.<sup>6</sup> AV, Atrioventricular; CHF, congestive heart failure; HR, heart rate; ICP, intracranial pressure; PE, pulmonary embolism; SA, sinoatrial; SVT, supraventricular tachycardia.

**FIGURE 7-9**

Supraventricular arrhythmias. p<sup>1</sup>, Premature atrial contraction. (From Park MK, Guntheroth WG. *How to Read Pediatric ECGs*. 4th ed. Philadelphia: Mosby; 2006:129.)

7

**FIGURE 7-10**

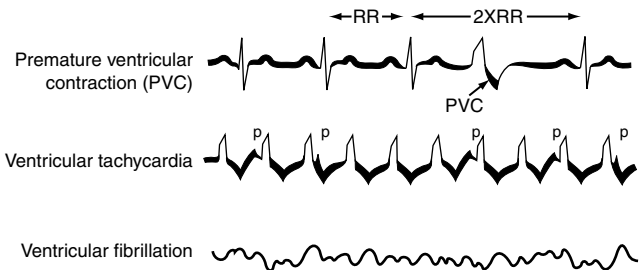
Supraventricular tachycardia pathway: Mechanism for orthodromic reentry tract (ORT), (i.e., Wolff-Parkinson-White [WPW]). Diagram shows sinoatrial (SA) node (*upper left circle*), with atrioventricular (AV) node (*above horizontal line*) and bundle branches crossing to ventricle (*below horizontal line*). (Adapted from Walsh EP. *Cardiac arrhythmias*. In: Fyler DC, ed. *Nadas' Pediatric Cardiology*. Philadelphia: Hanley & Belfus; 1992:384.)

TABLE 7-7

**VENTRICULAR ARRHYTHMIAS**

Name/Description	Cause	Treatment
<b>PREMATURE VENTRICULAR CONTRACTION (PVC)</b>		
Ectopic ventricular focus causing early depolarization. Abnormally wide QRS complex appears prematurely, usually with full compensatory pause. May be unifocal or multifocal.	Myocarditis, myocardial injury, cardiomyopathy, long QT, congenital and acquired heart disease, drugs (catecholamines, theophylline, caffeine, anesthetics), MVP, anxiety, hypokalemia, hypoxia, hypomagnesemia.	None. More worrisome if associated with underlying heart disease or syncope, if worse with activity, or if they are multiform (especially couplets).
<b>Bigeminy:</b> Alternating normal and abnormal QRS complexes.		Address underlying cause, rule out structural heart disease.
<b>Trigeminy:</b> Two normal QRS complexes followed by an abnormal one.	Can be normal variant.	
<b>Couplet:</b> Two consecutive PVCs.		
<b>VENTRICULAR TACHYCARDIA</b>		
Series of three or more PVCs at rapid rate (120–250 beats/min), with wide QRS complex and dissociated, retrograde, or no P wave	See causes of PVCs (70% have underlying cause).	See “Tachycardia with Poor Perfusion” and “Tachycardia with Adequate Perfusion” algorithms in back of handbook.
<b>VENTRICULAR FIBRILLATION</b>		
Depolarization of ventricles in uncoordinated asynchronous pattern, yielding abnormal QRS complexes of varying size and morphology with irregular, rapid rate. Rare in children.	Myocarditis, MI, postoperative state, digitalis or quinidine toxicity, catecholamines, severe hypoxia, electrolyte disturbances, long QT	Requires immediate defibrillation. See algorithm for “Asystole and Pulseless Arrest” at back of book.

MI, Myocardial infarction; MVP, mitral valve prolapse.



**FIGURE 7-11**

Ventricular arrhythmias. p, p wave, RR, R-R interval. (From Park MK, Guntheroth WG. How to Read Pediatric ECGs. 4th ed. Philadelphia: Mosby; 2006:138.)

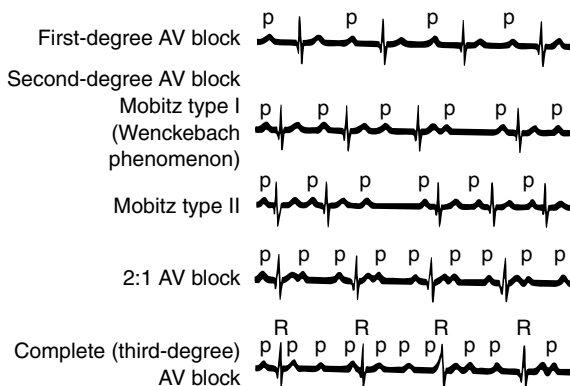


FIGURE 7-12

Conduction blocks. p, p wave; R, QRS complex. (From Park MK, Guntheroth WG. How to Read Pediatric ECGs. 4th ed. Philadelphia: Mosby; 2006:141.)

TABLE 7-8

## NONVENTRICULAR CONDUCTION DISTURBANCES

Name/Description*	Cause	Treatment
<b>FIRST-DEGREE HEART BLOCK</b>		
Abnormal but asymptomatic delay in conduction through AV node, yielding prolongation of PR interval	Acute rheumatic fever, tickborne (i.e., Lyme) disease, connective tissue disease, congenital heart disease, cardiomyopathy, digitalis toxicity, postoperative state, normal children	No specific treatment except address the underlying cause
<b>SECOND-DEGREE HEART BLOCK: MOBITZ TYPE I (WENCKEBACH)</b>		
Progressive lengthening of PR interval until a QRS complex is not conducted. Common finding in asymptomatic teenagers.	Myocarditis, cardiomyopathy, congenital heart disease, postoperative state, MI, toxicity (digitalis, $\beta$ -blocker), normal children, Lyme disease, lupus	Address underlying cause, or none needed
<b>SECOND-DEGREE HEART BLOCK: MOBITZ TYPE II</b>		
Loss of conduction to ventricle without lengthening of the PR interval. May progress to complete heart block.	Same as for Mobitz type I	Address underlying cause; may need pacemaker
<b>THIRD-DEGREE (COMPLETE) HEART BLOCK</b>		
Complete dissociation of atrial and ventricular conduction, with atrial rate faster than ventricular rate. P wave and PP interval regular; RR interval regular and much slower.	Congenital due to maternal lupus or other connective tissue disease	If bradycardic and symptomatic, consider pacing; see bradycardia algorithm at back of book.

\*High-degree AV block: Conduction of atrial impulse at regular intervals, yielding 2:1 block (two atrial impulses for each ventricular response), 3:1 block, etc.

AV, Atrioventricular; MI, myocardial infarction.

**TABLE 7-9****VENTRICULAR CONDUCTION DISTURBANCES**

Name/Description	Criteria	Causes/Treatment
<b>RIGHT BUNDLE-BRANCH BLOCK (RBBB)</b>		
Delayed right bundle conduction prolongs RV depolarization time, leading to wide QRS.	<ol style="list-style-type: none"> <li>1. Prolonged or wide QRS with terminal slurred R' (m-shaped RSR' or RR') in V<sub>1</sub>, V<sub>2</sub>, aVR</li> <li>2. Wide and slurred S wave in leads I and V<sub>6</sub></li> </ol>	ASD, surgery with right ventriculotomy, occasionally seen in normal children
<b>LEFT BUNDLE-BRANCH BLOCK (LBBB)</b>		
Delayed left bundle conduction prolongs septal and LV depolarization time, leading to wide QRS with loss of usual septal signal; there is still a predominance of left ventricle forces. Rare in children.	<ol style="list-style-type: none"> <li>1. Wide negative QS complex in lead V<sub>1</sub> with loss of septal R wave</li> <li>2. Wide R or RR' complex in lead V<sub>6</sub> with loss of septal Q wave</li> </ol>	Hypertension, ischemic or valvular heart disease, cardiomyopathy
<b>WOLFF-PARKINSON-WHITE (WPW)</b>		
Atrial impulse transmitted via anomalous conduction pathway to ventricles, bypassing AV node and normal ventricular conduction system. Leads to early and prolonged depolarization of ventricles. Bypass pathway is a predisposing condition for SVT.	<ol style="list-style-type: none"> <li>1. Shortened PR interval</li> <li>2. Delta wave</li> <li>3. Wide QRS</li> </ol>	Acute management of SVT if necessary as previously described; consider ablation of accessory pathway if recurrent SVT. All patients need cardiology referral.

ASD, Atrial septal defect; LV, left ventricle; RV, right ventricle; SVT, supraventricular tachycardia.

## C. ECG Findings Secondary to Electrolyte Disturbances, Medications, and Systemic Illnesses (Table 7-10)<sup>7,20</sup>

### D. Long QT

#### 1. **Diagnosis:**

- In general, QTc is similar in males and females from birth until late adolescence (0.37–0.44 sec).
- In adults, prolonged QTc is > 0.45 sec for males and > 0.45–0.46 sec for females.
- In approximately 10% of cases, patients may have a normal QTc on ECG. Patients may also have a family history of long QT with unexplained syncope, seizure, or cardiac arrest without prolongation of QTc on ECG.
- Treadmill exercise test may prolong the QTc and will sometimes incite arrhythmias.

- Complications:** Associated with ventricular arrhythmias (torsades de pointes), syncope, and sudden death

#### 3. **Management:**

- Congenital long QT:  $\beta$ -blockers and/or defibrillators; rarely require cardiac sympathetic denervation or cardiac pacemakers

TABLE 7-10

## SYSTEMIC EFFECTS ON ELECTROCARDIOGRAM

	Short QT	Long QT-U	Prolonged QRS	ST-T Changes	Sinus Tachycardia	Sinus Bradycardia	AV Block	Ventricular Tachycardia	Miscellaneous
<b>CHEMISTRY</b>									
Hyperkalemia			X	X			X	X	Low-voltage Ps; peaked Ts
Hypokalemia		X		X					
Hypercalcemia	X					X	X	X	
Hypocalcemia		X			X		X		
Hypermagnesemia							X		
Hypomagnesemia		X							
<b>DRUGS</b>									
Digitalis	X			X		T	X	T	
Phenothiazines		T						T	
Phenytoin	X								
Propranolol	X					X	X		
Tricyclics		T	T	T	T		T	T	
Verapamil						X	X		

Continued

TABLE 7-10

## SYSTEMIC EFFECTS ON ELECTROCARDIOGRAM (Continued)

	Short QT	Long QT-U	Prolonged QRS	ST-T Changes	Sinus Tachycardia	Sinus Bradycardia	AV Block	Ventricular Tachycardia	Miscellaneous
<b>MISCELLANEOUS</b>									
CNS injury		X		X	X	X	X		
Friedreich ataxia				X	X				Atrial flutter
Duchenne muscular dystrophy					X	X			Atrial flutter
Myotonic dystrophy			X	X	X		X		
Collagen vascular disease				X			X	X	
Hypothyroidism						X			Low voltage
Hyperthyroidism			X	X	X		X		
Lyme disease			X				X		
Holt-Oram, maternal lupus							X		

CNS, Central nervous system; T, present only with drug toxicity; X, present.

Adapted from Garson A Jr. *The Electrocardiogram in Infants and Children: A Systematic Approach*. Philadelphia: Lea & Febiger; 1983:172; and Walsh EP. Cardiac arrhythmias. In: Fyler DC, Nadas A, eds. *Pediatric Cardiology*. Philadelphia: Hanley & Belfus; 1992:141-143.

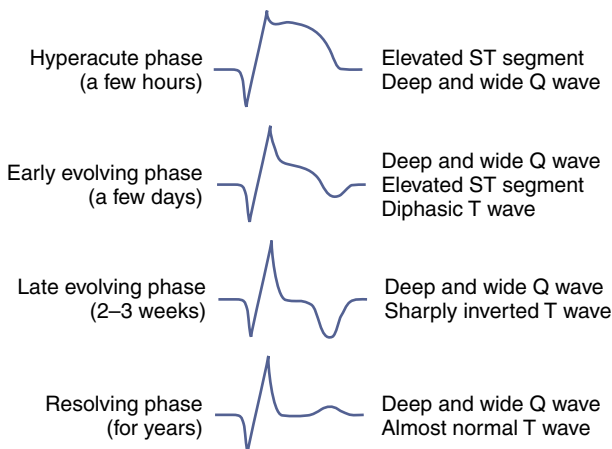
- b. Acquired long QT: Treatment of arrhythmias, discontinue precipitating drug, correction of metabolic abnormalities

**E. Hyperkalemia: ECG changes dependent on serum K<sup>+</sup> level; may have normal ECG with level between 2.5 and 6**

1. **Serum K<sup>+</sup> <2.5:** Depressed ST segment, diphasic T wave
2. **Serum K<sup>+</sup> >6:** Tall T wave
3. **Serum K<sup>+</sup> >7.5:** Long PR interval, wide QRS, tall T wave
4. **Serum K<sup>+</sup> >9:** Absent P wave, sinusoidal

**F. Myocardial Infarction (MI) in Children**

1. **Etiology:** Anomalous origin or aberrant course of a coronary artery, Kawasaki disease, congenital heart disease (presurgical and postsurgical), and dilated cardiomyopathy. Less often associated with hypertension, lupus, myocarditis, cocaine ingestion, and use of adrenergic drugs (e.g.,  $\beta$ -agonists used for asthma). Rare in children.
2. **Frequent ECG findings in children with acute MI<sup>9,10</sup>** (Fig. 7-13):
  - a. New-onset wide Q waves (>0.035 sec) seen within first few hours (persist over several years)
  - b. ST-segment elevation (>2 mm) seen within first few hours
  - c. Diphasic T waves seen within first few days (becoming sharply inverted, then normalizing over time)
  - d. Prolonged QTc interval (>0.44 sec) with abnormal Q waves



**FIGURE 7-13**

Sequential changes during myocardial infarction. (From Park MK, Guntheroth WG. How to Read Pediatric ECGs. 4th ed. Philadelphia: Mosby; 2006:115.)



e. Deep, wide Q waves in leads I, aVL, or V<sub>6</sub>, without Q waves in II, III, aVF, suggest anomalous origin of the left coronary artery.

### 3. **Other criteria:**

- Elevated creatine kinase (CK)/MB fraction: Not specific for acute MI in children
- Cardiac troponin I: More sensitive indicator of early myocardial damage in children.<sup>10</sup> Becomes elevated within hours of cardiac injury, persists for 4–7 days, is specific for cardiac injury.

## V. IMAGING

### A. Chest Radiograph

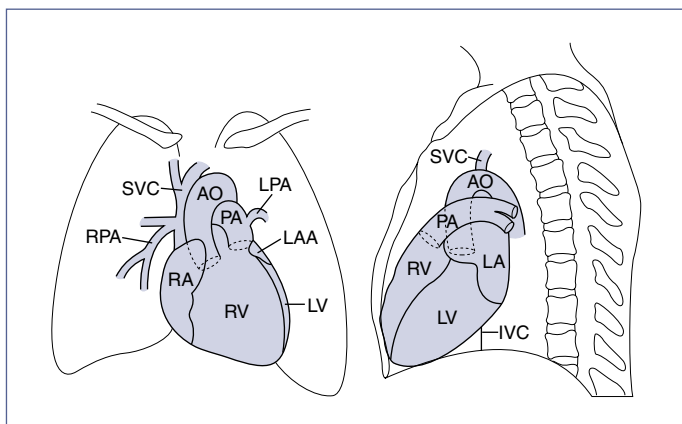
Please see Chapter 25 for more information on the chest radiograph.

#### 1. **Evaluate the heart:**

- Size: Cardiac shadow should be <50% of thoracic width (maximal width between inner margins of ribs, as measured on a posteroanterior radiograph during inspiration)
- Shape: Can aid in diagnosis of chamber/vessel enlargement and some congenital heart disease (Fig. 7-14)
- Situs (levocardia, mesocardia, dextrocardia)

#### 2. **Evaluate the lung fields:**

- Decreased pulmonary blood flow: Seen in pulmonary or tricuspid stenosis/atresia, TOF, pulmonary hypertension (peripheral pruning)
- Increased pulmonary blood flow: Seen as increased pulmonary vascular markings (PVMs) with redistribution from bases to apices of lungs and extension to lateral lung fields (see Tables 7-12 and 7-13)



**FIGURE 7-14**

Radiologic contours of the heart. AO, Aorta; IVC, inferior vena cava; LA, left atrium; LAA, left atrial appendage; LPA, left pulmonary artery; LV, left ventricle; PA, pulmonary artery; RA, right atrium; RPA, right pulmonary artery; RV, right ventricle; SVC, superior vena cava.

- c. Venous congestion, or congestive heart failure (CHF): Increased PVMs centrally, interstitial and alveolar pulmonary edema (air bronchograms), septal lines, and pleural effusions (see [Tables 7-12 and 7-13](#))
- 3. **Evaluate the trachea:** Usually bends slightly to the right above the carina in normal patients with a left-sided aortic arch. A perfectly straight or left-bending trachea suggests a right aortic arch, which may be associated with other defects (TOF, truncus arteriosus, vascular rings, chromosome 22 microdeletion).
- 4. **Skeletal anomalies:**
  - a. Rib notching (e.g., from collateral vessels in patients >5 years of age with coarctation of the aorta)
  - b. Sternal abnormalities (e.g., Holt-Oram syndrome, pectus excavatum in Marfan, Ehlers-Danlos, and Noonan syndromes)
  - c. Vertebral anomalies (e.g., VATER/VACTERL syndrome: **V**ertebral anomalies, **A**nal atresia, **T**racheoesophageal fistula, **R**adial and **R**enal, **C**ardiac, and **L**imb anomalies)

## B. Echocardiography

- 1. **Approach:**
  - a. Transthoracic echocardiography (TTE): Does not require general anesthesia, is simpler to perform than transesophageal echocardiography (TEE), but does have limitations in some patients (e.g., uncooperative, obese, or those with suspected endocarditis)
  - b. TEE: Uses an ultrasound transducer on the end of a modified endoscope to view the heart from the esophagus and stomach, allowing for better imaging of intracardiac structures. TEE allows for better imaging in obese and intraoperative patients and is also useful for visualizing very small lesions, such as some vegetations.
- 2. **Shortening fraction:** Very reliable index of left ventricular function. Normal values range from 30%–45%, depending on age.<sup>11</sup> For more information on echocardiography see Expert Consult, Chapter 7.

## C. Cardiac Catheterization

See [Fig. EC 7-A](#) for diagram of normal pressure values.

# VI. CONGENITAL HEART DISEASE

## A. Pulse Oximetry Screening for Critical Congenital Heart Disease

- 1. **Recommended after 24 hours of life or as late as possible if earlier discharge from the nursery.** There is a lower false-positive rate after 24 hours of life.
- 2. **Screening recommended on the right hand and on one foot,** either in parallel or direct sequence.
- 3. **Screening result would be considered positive if:**
  - a. Any oxygen saturation measure is < 90%.
  - b. Oxygen saturation is <95% in both extremities on 3 measures, each separated by 1 hour.

## 3. Modes

- M mode: *Ice pick view*—limited ability to show spatial structural relationship. Replaced by two-dimensional echo. Currently still used to measure dimensions of vessels and heart chambers, evaluate for pericardial effusion, assess valve motion, left ventricular (LV) systolic function.
- Two-dimensional: Better demonstration of spatial structure relationship
- Doppler: To demonstrate flow, cardiac output, and pressure gradients
- Shortening fraction: Evaluates LV systolic function. Formula:  $FS (\%) = \frac{Dd - Ds}{Dd} \times 100$  (Dd, End-diastolic dimension; Ds, end-systolic dimension). Normal value mean is 36%.

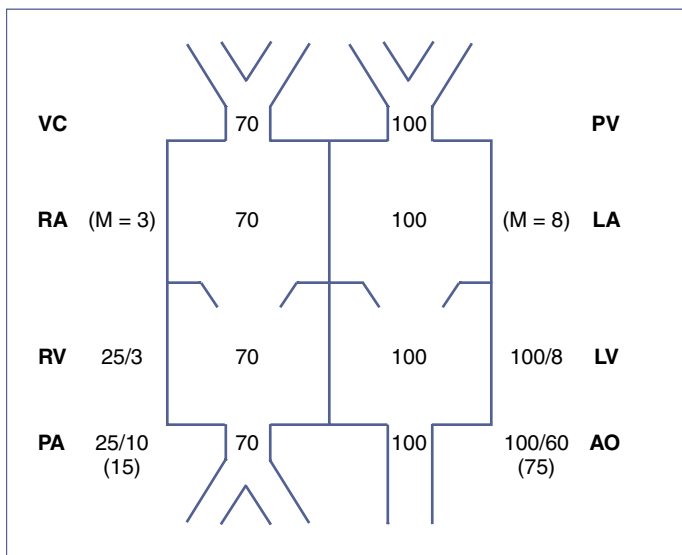


FIGURE EC 7-A

Cardiac catheterization: Diagram of normal pressure values. AO, Aorta; LA, left atrium; LV, left ventricle; PA, pulmonary artery; PV, pulmonary vein; RA, right atrium; RV, right ventricle; VC, venae cavae. (From Park MK. *Pediatric Cardiology for Practitioners*. 5th ed. St Louis: Mosby; 2008.)

- c. There is a >3% absolute difference in oxygen saturation between the right hand and foot on 3 measures, each separated by 1 hour.

**B. Common Syndromes Associated with Cardiac Lesions (Table 7-11)**

**C. Acyanotic Lesions (Table 7-12)**

**D. Cyanotic Lesions (Table 7-13)**

An oxygen challenge test is used to evaluate the etiology of cyanosis in neonates. Obtain baseline arterial blood gas (ABG) with saturation at  $\text{Fio}_2 = 0.21$ , then place infant in an oxygen hood at  $\text{Fio}_2 = 1$  for a minimum of 10 min, and repeat ABG. In cardiac disease, there will not be a significant change in  $\text{Pao}_2$  following the oxygen challenge test.

**Note:** Pulse oximetry will not be useful for following the change in oxygenation once the saturations reach 100% (approximately  $\text{Pao}_2 > 90$  mmHg).<sup>11-14</sup>

1. See Table EC 7-B for **interpretation of oxygen challenge test**.
2. Table 7-14 shows acute **management of hypercyanotic spells in TOF**.

**TABLE 7-11**

**MAJOR SYNDROMES ASSOCIATED WITH CARDIAC DEFECTS**

Syndrome	Dominant Cardiac Defect
CHARGE	TOF, truncus arteriosus, aortic arch abnormalities
DiGeorge	Aortic arch anomalies, TOF, truncus arteriosus, VSD, PDA
Trisomy 21	Atrioventricular septal defect, VSD
Marfan	Aortic root dilation, mitral valve prolapse
Loeys-Dietz	Aortic root dilation with higher risk of rupture at smaller dimensions
Noonan	Supravalvular pulmonic stenosis, LVH
Turner	COA, bicuspid aortic valve, aortic root dilation as a teenager
Williams	Supravalvular aortic stenosis, pulmonary artery stenosis
FAS	Occasional: VSD, PDA, ASD, TOF
IDM	TGA, VSD, COA, cardiomyopathy
VATER/VACTERL	VSD
VCFS	Truncus arteriosus, TOF, pulmonary atresia with VSD, TGA, interrupted aortic arch

ASD, Atrial septal defect; CHARGE, a syndrome of associated defects including Coloboma of the eye, Heart anomaly, choanal Atresia, Retardation, and Genital and Ear anomalies; COA, coarctation of aorta; FAS, fetal alcohol syndrome; IDM, infant of diabetic mother; LVH, left ventricular hypertrophy; PDA, patent ductus arteriosus; TGA, transposition of the great arteries; TOF, tetralogy of Fallot; VATER/VACTERL, association of Vertebral anomalies, Anal atresia, Cardiac anomalies, Tracheoesophageal fistula, Renal/radial anomalies, Limb defects; VCFS, velocardiofacial syndrome; VSD, ventricular septal defect.

Adapted from Park MK. *Pediatric Cardiology for Practitioners*. 5th ed. St Louis: Mosby; 2008:10-12.

TABLE EC 7-B

## INTERPRETATION OF OXYGEN CHALLENGE TEST

Condition	$F_{iO_2} = 0.21$ $P_{aO_2}$ (% Saturation)	$F_{iO_2} = 1.00$ $P_{aO_2}$ (% Saturation)	$P_{aCO_2}$
Normal	70 (95)	>200 (100)	35
Pulmonary disease	50 (85)	>150 (100)	50
Neurologic disease	50 (85)	>150 (100)	50
Methemoglobinemia	70 (85)	>200 (85)	35
Cardiac disease			
• Separate circulation*	<40 (<75)	<50 (<85)	35
• Restricted PBF†	<40 (<75)	<50 (<85)	35
• Complete mixing without restricted PBF‡	50 (85)	<150 (<100)	35
Persistent pulmonary hypertension	<i>Preductal</i>	<i>Postductal</i>	
PFO (no R–L shunt)	70 (95)	<40 (<75) Variable	35–50
PFO (with R–L shunt)	<40 (<75)	<40 (<75) Variable	35–50

\*D-Transposition of the great arteries (D-TGA) with intact ventricular septum.

†Tricuspid atresia with pulmonary stenosis or atresia, pulmonary atresia or critical pulmonary stenosis with intact ventricular septum, or tetralogy of Fallot.

‡Truncus, total anomalous pulmonary venous return, single ventricle, hypoplastic left heart, D-TGA with ventricular septal defect, tricuspid atresia without pulmonary stenosis or atresia.

PBF, Pulmonary blood flow; PFO, patent foramen ovale.

Adapted from Lees MH. Cyanosis of the newborn infant: Recognition and clinical evaluation. *J Pediatr*. 1970;77:484; Kitterman JA. Cyanosis in the newborn infant. *Pediatr Rev*. 1982;4:13; and Jones RW, Baumer JH, Joseph MC, et al. Arterial oxygen tension and response to oxygen breathing in differential diagnosis of heart disease in infancy. *Arch Dis Child*. 1976;51:667-673.

TABLE 7-12

## ACYANOTIC CONGENITAL HEART DISEASE

Lesion Type	% of CHD/Examination Findings	CDG Findings	Chest Radiograph Findings
Ventricular septal defect (VSD)	2–5/6 holosystolic murmur, loudest at the LLSB, $\pm$ systolic thrill $\pm$ apical diastolic rumble with large shunt With large VSD and pulmonary hypertension, $S_2$ may be narrow	<i>Small VSD</i> : Normal <i>Medium VSD</i> : LVH $\pm$ LAE <i>Large VSD</i> : BVH $\pm$ LAE, pure RVH	May show cardiomegaly and increased PVMs, depending on amount of left-to-right shunting
Atrial septal defect (ASD)	Wide, fixed split $S_2$ with grade 2–3/6 SEM at the LUSB May have mid-diastolic rumble at LLSB	<i>Small ASD</i> : Normal <i>Large ASD</i> : RAD and mild RVH or RBBB with RSR' in $V_1$	May show cardiomegaly with increased PVMs if hemodynamically significant ASD
Patent ductus arteriosus (PDA)	40%–60% in VLBW infants 1–4/6 continuous “machinery” murmur loudest at LUSB Wide pulse pressure	<i>Small–moderate PDA</i> : Normal or LVH <i>Large PDA</i> : BVH	May have cardiomegaly and increased PVMs, depending on size of shunt (see Chapter 18 Section IX.A for treatment)
Atrioventricular septal defects	Most occur in Down syndrome Hyperactive precordium with systolic thrill at LLSB and loud $S_2 \pm$ grade 3–4/6 holosystolic regurgitant murmur along LLSB $\pm$ systolic murmur of MR at apex $\pm$ mid-diastolic rumble at LLSB or at apex $\pm$ gallop rhythm	Superior QRS axis RVH and LVH may be present	Cardiomegaly with increased PVMs
Pulmonary stenosis (PS)	Ejection click at LUSB with valvular PS—click intensity varies with respiration, decreasing with inspiration and increasing with expiration $S_2$ may split widely with $P_2$ diminished in intensity SEM (2–5/6) $\pm$ thrill at LUSB with radiation to back and sides	<i>Mild PS</i> : Normal <i>Moderate PS</i> : RAD and RVH <i>Severe PS</i> : RAE and RVH with strain	Normal heart size with normal to decreased PVMs
Aortic stenosis (AS)	Systolic thrill at RUSB, suprasternal notch, or over carotids Ejection click that does not vary with respiration if valvular AS Harsh SEM (2–4/6) at second RICS or third LICS, with radiation to neck and apex $\pm$ early diastolic decrescendo murmur due to AR Narrow pulse pressure if severe stenosis	<i>Mild AS</i> : Normal <i>Moderate–severe AS</i> : LVH $\pm$ strain	Usually normal

TABLE 7-12

## ACYANOTIC CONGENITAL HEART DISEASE (Continued)

Lesion Type	% of CHD/Examination Findings	CDG Findings	Chest Radiograph Findings
Coarctation of aorta may present as:	Male/female ratio of 2:1 2–3/6 SEM at LUSB, radiating to left interscapular area	<i>In infancy:</i> RVH or RBBB <i>In older children:</i> LVH	Marked cardiomegaly and pulmonary venous congestion. Rib notching from collateral circulation usually not seen in children younger than 5 years because collaterals not yet established.
1. Infant in CHF	Bicuspid valve is often associated, so may have systolic ejection click at apex and RUSB		
2. Child with HTN	BP in lower extremities will be lower than in upper extremities.		
3. Child with murmur	Pulse oximetry discrepancy of >5% between upper and lower extremities is also suggestive of coarctation.		

AR, Aortic regurgitation; ASD, atrial septal defect; BP, blood pressure; BVH, biventricular hypertrophy; CHD, congenital heart disease; CHF, congestive heart failure; HTN, hypertension; LAE, left atrial enlargement; LICs, left intercostal space; LLSB, left lower sternal border; LUSB, left upper sternal border; LVH, left ventricular hypertrophy; MR, mitral regurgitation; PVM, pulmonary vascular markings; RAD, right axis deviation; RAE, right atrial enlargement; RBBB, right bundle-branch block; RICS, right intercostal space; RUSB, right upper sternal border; RVH, right ventricular hypertrophy; SEM, systolic ejection murmur; VLBW, very low birth weight (i.e. <1500 g); VSD, ventricular septal defect.

TABLE 7-13

## CYANOTIC CONGENITAL HEART DISEASE

Lesion	Examination Findings	ECG Findings	Chest Radiograph Findings
Tetralogy of Fallot:			
1. Large VSD	Loud SEM at LMSB and LUSB and a loud, single S <sub>2</sub> ± thrill at LMSB and LLSB.	RAD and RVH	Boot-shaped heart with normal heart size ± decreased PVMs
2. RVOT obstruction			
3. RVH			
4. Overriding aorta	<i>Tet spells:</i> Occur in young infants. As RVOT obstruction increases or systemic resistance decreases, right-to-left shunting across VSD occurs. May present with tachypnea, increasing cyanosis, and decreasing murmur. See <a href="#">Table 7-14</a> for treatment.		
Degree of RVOT obstruction will determine whether there is clinical cyanosis. If PS is mild, there will be a left-to-right shunt, and child will be acyanotic. Increased obstruction leads to increased right-to-left shunting across VSD, and child will be cyanotic.			

TABLE 7-13

## CYANOTIC CONGENITAL HEART DISEASE (Continued)

Lesion	Examination Findings	ECG Findings	Chest Radiograph Findings
Transposition of great arteries	Nonspecific. Extreme cyanosis. Loud, single $S_2$ . No murmur unless there is associated VSD or PS.	RAD and RVH (due to RV acting as systemic ventricle). Upright T wave in $V_1$ after age 3 days may be only abnormality.	Classic finding: "egg on a string" with cardiomegaly; possible increased PVMs
Tricuspid atresia: Absent tricuspid valve and hypoplastic RV and PA. Must have ASD, PDA, or VSD to survive.	Single $S_2$ + grade 2–3/6 systolic regurgitation murmur at LLSB if VSD is present. Occasional PDA murmur.	Superior QRS axis; RAE or CAE and LVH	Normal or slightly enlarged heart size; may have boot-shaped heart
Total anomalous pulmonary venous return Instead of draining into LA, pulmonary veins drain into the following locations. Must have ASD or PFO for survival:	Hyperactive RV impulse, quadruple rhythm, $S_2$ fixed and widely split, 2–3/6 SEM at LUSB, and mid-diastolic rumble at LLSB	RAD, RVH (RSR' in $V_1$ ). May see RAE	Cardiomegaly and increased PVMs; classic finding is "snowman in a snowstorm," but this is rarely seen until after age 4 months.
<ol style="list-style-type: none"> <li>1. <i>Supracardiac (most common):</i> SVC</li> <li>2. <i>Cardiac:</i> Coronary sinus or RA</li> <li>3. <i>Subdiaphragmatic:</i> IVC, portal vein, ductus venosus, or hepatic vein</li> <li>4. <i>Mixed type</i></li> </ol>			

## OTHER

Cyanotic CHDs that occur at a frequency of <1% each include pulmonary atresia, Ebstein anomaly, truncus arteriosus, single ventricle, and double outlet right ventricle

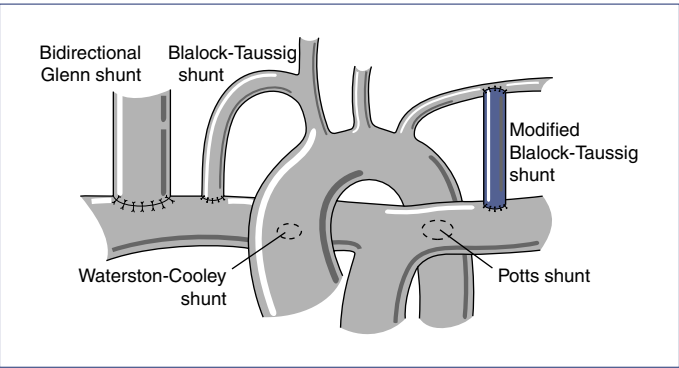
ASD, Atrial septal defect; CAE, common atrial enlargement; ECG, electrocardiogram; IVC, inferior vena cava; LA, left atrium; LLSB, left lower sternal border; LMSB, left mid-sternal border; LUSB, left upper sternal border; LVH, left ventricular hypertrophy; PA, pulmonary artery; PDA, patent ductus arteriosus; PFO, patent foramen ovale; PVM, pulmonary vascular markings; PS, pulmonary stenosis; RA, right atrium; RAD, right-axis deviation; RAE, right atrial enlargement; RV, right ventricle; RVH, right ventricular hypertrophy; RVOT, right ventricular outflow tract; SEM, systolic ejection murmur; SVC, superior vena cava; VSD, ventricular septal defect.



**TABLE 7-14**  
**TREATMENT OPTIONS FOR TET SPELLS**

Treatment	Rationale
<b>INITIAL OPTIONS</b>	
Calm child	Decreases PVR
Encourage knee-chest position	Decreases venous return and increases SVR
Oxygen	Reduces hypoxemia, decreases PVR
Intravenous fluids	Provides volume resuscitation
Morphine (morphine sulfate 0.1–0.2 mg/kg SQ or IM)	Decreases venous return, decreases PVR, relaxes infundibulum. Do <i>not</i> try to establish IV access initially; use SQ route.
<b>IF THERE IS NO RESPONSE TO INITIAL MEASURES</b>	
Phenylephrine (0.02 mg/kg IV)	Increases SVR
Propranolol (0.01–0.25 mg/kg slow IV push)	Has negative inotropic effect on infundibular myocardium; may block drop in SVR
Ketamine 1–3 mg/kg	Increases SVR and sedates
<b>OTHER</b>	
Correct anemia	Increases delivery of oxygen to tissues
Correct pathologic tachyarrhythmias	May abort hypoxic spell
Infuse glucose	Avoids hypoglycemia from increased utilization and depletion of glycogen stores

IM, Intramuscular; IV, intravenous; PVR, peripheral venous resistance; SQ, subcutaneous; SVR, systemic vascular resistance.  
From Park MK. *Pediatric Cardiology for Practitioners*. 5th ed. St Louis: Mosby; 2008:239.



**FIGURE 7-15**  
Schematic diagram of cardiac shunts.

**E. Surgeries and Other Interventions (Fig. 7-15)**

1. **Atrial septostomy:** Creates an intra-atrial opening to allow for mixing or shunting between atria of systemic and pulmonary venous blood. Used for transposition of the great arteries (TGA), tricuspid, mitral, tricuspid and pulmonary atresia, and sometimes total anomalous pulmonary venous return. Most commonly performed percutaneously with a balloon-tipped catheter (Rashkind procedure).

2. **Palliative systemic-to-pulmonary artery shunts**, such as the Blalock-Taussig shunt (subclavian artery to pulmonary artery [PA]): Use systemic arterial flow to increase pulmonary blood flow in cardiac lesions with impaired pulmonary perfusion (e.g., TOF, hypoplastic right heart, tricuspid atresia, pulmonary atresia)
3. **Palliative superior vena cava-to-pulmonary artery shunts**, such as the Glenn shunt, also known as the *hemi-Fontan* (superior vena cava [SVC] to the right pulmonary artery [RPA]): Directs a portion of the systemic venous return directly into the pulmonary blood flow as an intermediate step to a Fontan procedure. This procedure is usually performed outside the neonatal period, when there is lower pulmonary vascular resistance.
4. **Fontan procedure**: Performed after the Glenn shunt; involves anastomosis of the right atria and/or inferior vena cava (IVC) to pulmonary arteries via conduits; separates systemic and pulmonary circulations in patients with functionally single ventricles (tricuspid atresia, hypoplastic left heart syndrome)
5. **Norwood procedure**: Used for hypoplastic left heart syndrome
  - a. Stage 1 (neonatal period): To provide systemic blood flow, anastomosis of the proximal main pulmonary artery (MPA) is made to the aorta, with aortic arch reconstruction and patch closure of the distal MPA. To provide pulmonary blood flow, a modified right Blalock-Taussig shunt (subclavian artery to RPA) or Sano modification (RV to PA conduit) is performed. An atrial septal defect is created if needed to decompress the left atrium and allow for adequate left-to-right flow. Expected  $O_2$  saturations: 75%–85%.
  - b. Stage 2 (3–6 months of age): Bidirectional Glenn shunt or hemi-Fontan to reduce volume overload of single right ventricle. Expected  $O_2$  saturations: 80%–85%.
  - c. Modified Fontan (age 18 mo–4 yr): Needed to completely separate systemic and pulmonary circulations. Restores normal  $O_2$  saturation, with expected  $O_2$  saturation >92%.
6. **Arterial switch procedure**: Used for repair of TGA. Connects aorta to left ventricle and pulmonary artery to right ventricle. Procedure also involves reconnecting coronary arteries to aorta.
7. **Ross procedure**: Pulmonary root autograft for aortic stenosis; autologous pulmonary valve replaces aortic valve, and aortic or pulmonary allograft replaces pulmonary valve.



## VII. ACQUIRED HEART DISEASE

### A. Endocarditis

1. **Common causative organisms**: About 70% of causes of endocarditis are streptococcal species (*Streptococcus viridans*, enterococci); 20% are staphylococcal species (*Staphylococcus aureus*, *Staphylococcus epidermidis*); 10% are other organisms (*Haemophilus influenzae*, gram-negative bacteria, fungi).

2. **Clinical findings:** New heart murmur, recurrent fever, splenomegaly, petechiae, fatigue, Osler nodes (tender nodules at fingertips), Janeway lesions (painless hemorrhagic areas on palms or soles), splinter hemorrhages, and Roth spots (retinal hemorrhages)

### B. Bacterial Endocarditis Prophylaxis

See [Table 7-15](#) for antibiotic choices and [Box 7-4](#) for cardiac conditions requiring prophylaxis.<sup>15</sup>

1. **All dental procedures** that involve treatment of gingival tissue or periapical region of the teeth or oral mucosal perforation
2. **Invasive procedures** that involve incision or biopsy of respiratory mucosa, such as tonsillectomy and adenoidectomy
3. **Not recommended** for genitourinary or gastrointestinal tract procedures; solely for bacterial endocarditis prevention

### C. Myocardial Disease

1. **Dilated cardiomyopathy:** End result of myocardial damage, leading to atrial and ventricular dilation with decreased systolic contractile function of the ventricles
  - a. Etiology: Infectious, toxic (alcohol, anthracyclines), metabolic (hypothyroidism, muscular dystrophy), immunologic, collagen vascular disease, nutritional deficiency (kwashiorkor, beriberi)
  - b. Symptoms: Fatigue, weakness, shortness of breath
  - c. Examination: Look for signs of CHF(e.g., tachycardia, tachypnea, rales, cold extremities, jugular venous distention, hepatomegaly, peripheral edema, S<sub>3</sub> gallop, displacement of point of maximal impulse to the left and inferiorly)
  - d. Chest radiograph: Generalized cardiomegaly, pulmonary congestion
  - e. ECG: Sinus tachycardia, left ventricular hypertrophy (LVH), possible atrial enlargement, arrhythmias, conduction disturbances, ST-segment and T-wave changes

**TABLE 7-15**

#### PROPHYLACTIC REGIMENS FOR DENTAL AND RESPIRATORY TRACT PROCEDURES

Drug	Dosing* (not to exceed adult dose)
Amoxicillin†	Adult: 2 g; Child: 50 mg/kg PO
Ampicillin	Adult: 2 g; Child: 50 mg/kg IM/IV
Cefazolin or ceftriaxone‡	Adult: 1 g; Child: 50 mg/kg IM/IV
Cephalexin‡	Adult: 2 g; Child: 50 mg/kg PO
Clindamycin	Adult: 600 mg; Child: 20 mg/kg PO/IM/IV
Azithromycin/clarithromycin	Adult: 500 mg; Child: 15 mg/kg PO

\*Oral (PO) medications should be given 1 hour before procedure; intramuscular/intravenous (IM/IV) medications should be given within 30 min prior to procedure.

†Standard general prophylaxis.

‡Cephalosporins should not be used in persons with intermediate-type hypersensitivity reaction to penicillins or ampicillin.

Adapted from Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis: Guidelines from the American Heart Association: A guideline from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. *Circulation*. 2007;116:1736-1754.

## BOX 7-4

**CARDIAC CONDITIONS FOR WHICH ANTIBIOTIC PROPHYLAXIS IS RECOMMENDED FOR DENTAL, RESPIRATORY TRACT, INFECTED SKIN, SKIN STRUCTURES, OR MUSCULOSKELETAL TISSUE PROCEDURES**

- Prosthetic cardiac valve
- Previous bacterial endocarditis
- Congenital heart disease (CHD)—Limited to the following conditions\*
  - Unrepaired cyanotic defect, including palliative shunts and conduits
  - Completely repaired CHD with prosthetic material/device (placed by surgery or catheterization), during first 6 months after procedure†
  - Repaired CHD with residual defects at or adjacent to the site of prosthetic patch or device (which inhibit endothelialization)
  - Cardiac transplantation patients who develop cardiac valvulopathy

\*Conditions associated with the highest risk of adverse outcome from endocarditis.

†Endothelialization process of prosthetic material occurs within 6 months after the procedure.

Adapted from Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis: Guidelines from the American Heart Association: A guideline from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. *Circulation*. 2007;116:1736-1754.

- f. Echocardiography: Enlarged ventricles (increased end-diastolic and end-systolic dimensions) with little or no wall thickening; decreased shortening fraction
- g. Treatment: Management of CHF (digoxin, diuretics, vasodilation, angiotensin-converting enzyme [ACE] inhibitors, rest). Consider anticoagulants to decrease risk for thrombus formation.
2. **Hypertrophic cardiomyopathy:** Abnormality of myocardial cells leading to significant ventricular hypertrophy, particularly of left ventricle, with small to normal ventricular dimensions. Increased contractile function but impaired filling secondary to stiff ventricles. The most common type is asymmetrical septal hypertrophy, also called *idiopathic hypertrophic subaortic stenosis* (IHSS), with varying degrees of obstruction. A 4%–6% incidence of sudden death in children and adolescents with hypertrophic obstructive cardiomyopathy (HOCM).
  - a. Etiology: Genetic (autosomal dominant, 60% of cases) or sporadic (40% of cases)
  - b. Symptoms: Easy fatigability, anginal pain, shortness of breath, occasional palpitations
  - c. Examination: Usually in adolescents or young adults; signs include left ventricular heave, sharp upstroke of arterial pulse, murmur of mitral regurgitation, midsystolic ejection murmur along left midsternal border (LMSB) that increases in intensity in the standing position (in patients with midcavity left ventricular obstruction)
  - d. Chest radiograph: Globular-shaped heart with left ventricular enlargement
  - e. ECG: LVH, prominent Q waves (septal hypertrophy), ST-segment and T-wave changes, arrhythmias

- f. Echocardiography: Extent and location of hypertrophy, obstruction, increased contractility
- g. Treatment: Moderate restriction of physical activity, administration of negative inotropes ( $\beta$ -blocker, calcium channel blocker) to help improve filling and subacute bacterial endocarditis prophylaxis. If at increased risk for sudden death, may consider implantable defibrillator. If symptomatic with subaortic obstruction, may benefit from myectomy.
- 3. **Restrictive cardiomyopathy:** Myocardial or endocardial disease (usually infiltrative or fibrotic) resulting in stiff ventricular walls, with restriction of diastolic filling but normal contractile function. Results in atrial enlargement. Associated with a high mortality rate. Very rare in children.
  - a. Etiology: Scleroderma, amyloidosis, sarcoidosis, mucopolysaccharidosis
  - b. Treatment: Supportive, poor prognosis. Diuretics, anticoagulants, calcium channel blockers, pacemaker for heart block, cardiac transplantation if severe.
- 4. **Myocarditis:** Inflammation of myocardial tissue
  - a. Etiology: Viral (coxsackievirus, echovirus, adenovirus, poliomyelitis, mumps, measles, rubella, cytomegalovirus, HIV, arbovirus, influenza); bacterial, rickettsial, fungal, or parasitic infection; immune-mediated disease (Kawasaki disease, acute rheumatic fever); collagen vascular disease; toxin-induced
  - b. Symptoms: Nonspecific and inconsistent, depending on severity of disease. Variably anorexia, lethargy, emesis, lightheadedness, cold extremities, shortness of breath.
  - c. Examination: Look for signs of CHF (tachycardia, tachypnea, jugular venous distention, rales, gallop, hepatomegaly); occasionally a soft systolic murmur or arrhythmia may be noted.
  - d. Chest radiograph: Variable cardiomegaly and pulmonary edema
  - e. ECG: Low QRS voltages throughout ( $<5$  mm), ST-segment and T-wave changes (e.g., decreased T-wave amplitude), prolongation of QT interval, arrhythmias (especially premature contractions, first- or second-degree AV block)
  - f. Laboratory tests: CK, troponin
  - g. Echocardiography: Enlargement of heart chambers, impaired left ventricular function
  - h. Treatment: Bed rest, diuretics, inotropes (dopamine, dobutamine, milrinone), digoxin, gamma globulin (2 g/kg over 24 hours), ACE inhibitors, possibly steroids. May require heart transplantation if no improvement ( $\approx 20\%$ – $25\%$  of cases)

#### D. Pericardial Disease

- 1. **Pericarditis:** Inflammation of visceral and parietal layers of pericardium
  - a. Etiology: Viral (especially echovirus, coxsackievirus B), tuberculosis, bacterial, uremic, neoplastic, collagen vascular, post-MI or postpericardiotomy, radiation induced, drug induced (e.g., procainamide, hydralazine), or idiopathic

- b. Symptoms: Chest pain (retrosternal or precordial, radiating to back or shoulder, pleuritic in nature, alleviated by leaning forward, aggravated by supine position), dyspnea
  - c. Examination: Pericardial friction rub, distant heart sounds, fever, tachypnea
  - d. ECG: Diffuse ST-segment elevation in almost all leads (representing inflammation of adjacent myocardium); PR-segment depression
  - e. Treatment: Often self-limited. Treat underlying condition and provide symptomatic treatment with rest, analgesia, and antiinflammatory drugs
2. **Pericardial effusion:** Accumulation of excess fluid in pericardial sac
- a. Etiology: Associated with acute pericarditis (exudative fluid) or serous effusion resulting from increased capillary hydrostatic pressure (e.g., CHF), decreased plasma oncotic pressure (e.g., hypoproteinemia), and increased capillary permeability (transudative fluid)
  - b. Symptoms: Can present with no symptoms, dull ache in left chest, abdominal pain, or symptoms of cardiac tamponade (see later)
  - c. Examination: Muffled distant heart sounds, dullness to percussion of posterior left chest (secondary to atelectasis from large pericardial sac), hemodynamic signs of cardiac compression
  - d. Chest radiograph: Globular symmetrical cardiomegaly
  - e. ECG: Decreased voltage of QRS complexes, electrical alternans (variation of QRS axis with each beat secondary to swinging of heart within pericardial fluid)
  - f. Echocardiography shows extent and location of hypertrophy, obstruction, increased contractility
  - g. Treatment: Address underlying condition. Observe if asymptomatic; use pericardiocentesis if there is sudden increase in volume or hemodynamic compromise. Nonsteroidal antiinflammatory drugs (NSAIDs) or steroids may be of benefit, depending on etiology.
3. **Cardiac tamponade:** Accumulation of pericardial fluid under high pressure, causing compression of cardiac chambers, limiting filling, and decreasing stroke volume and cardiac output
- a. Etiology: Same as pericardial effusion; most commonly associated with viral infection, neoplasm, uremia, and acute hemorrhage
  - b. Symptoms: Dyspnea, fatigue, cold extremities
  - c. Examination: Jugular venous distention, hepatomegaly, peripheral edema, tachypnea, rales (from increased systemic and pulmonary venous pressure), hypotension, tachycardia, pulsus paradoxus (decrease in systolic blood pressure by  $>10$  mmHg with each inspiration), decreased capillary refill (from decreased stroke volume and cardiac output), quiet precordium, and muffled heart sounds
  - d. ECG: Sinus tachycardia, decreased voltage, electrical alternans
  - e. Echocardiography: Right ventricle collapse in early diastole, right atrial/left atrial collapse in end-diastole and early systole
  - f. Treatment: Pericardiocentesis with temporary catheter left in place if necessary (see Chapter 3, Figs. 3-15 and 3-16); pericardial window or stripping if it is a recurrent condition

## E. Kawasaki Disease

Acute febrile vasculitis of unknown etiology, common in children < 8 years of age, and the leading cause of acquired heart disease in children in developed countries

1. **Etiology:** Unknown; thought to be immune regulated in response to infectious agents or environmental toxins
2. **Diagnosis:**
  - a. Typical Kawasaki disease: Based on clinical criteria. These include high fever lasting 5 days or more, plus at least 4 of the following 5 criteria:
    - (1) Bilateral painless bulbar conjunctival injection without exudate
    - (2) Erythematous mouth and pharynx, strawberry tongue, or red cracked lips
    - (3) Polymorphous exanthem (may be morbilliform, maculopapular, or scarlatiniform)
    - (4) Swelling of hands and feet, with erythema of palms and soles
    - (5) Cervical lymphadenopathy (>1.5 cm in diameter), usually single and unilateral
  - b. Atypical/incomplete Kawasaki disease: A suspicion of Kawasaki but with fewer of the criteria required for diagnosis. Even without all criteria, there is a risk for coronary artery abnormalities.
    - (1) More often seen in infants. Echocardiography should be considered in any infant < 6 months with fever > 7 days duration, laboratory evidence of systemic inflammation, and no other explanation for the febrile illness.
    - (2) See [Fig. 7-16](#) for evaluation of incomplete Kawasaki disease.
    - (3) Supplemental laboratory criteria: Albumin  $\leq 3.0$  g/dL, anemia for age, elevation of alanine aminotransferase, platelets after 7 days  $\geq 450,000 / \text{mm}^3$ , white blood cell count  $\geq 15,000 / \text{mm}^3$ , and urine white blood cells/hpf  $\geq 10$ .
3. **Other clinical findings:** Often associated with extreme irritability, abdominal pain, diarrhea, vomiting. Also seen are arthritis and arthralgias, hepatic enlargement, jaundice, acute acalculous distention of the gallbladder, carditis, aseptic meningitis (50% of those undergoing LP).
4. **Laboratory findings:** Leukocytosis with left shift, neutrophils with vacuoles or toxic granules, elevated C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR) (seen acutely), thrombocytosis (after first week, peaking at 3 weeks), normocytic and normochromic anemia, sterile pyuria (33%), increased transaminases (40%), hyperbilirubinemia (10%)
5. **Subacute phase (11–25 days after onset of illness):** Resolution of fever, rash, and lymphadenopathy. Often, desquamation of the fingertips or toes and thrombocytosis occur.

Cardiovascular complications: If untreated, 20%–25% develop coronary artery aneurysms and dilation in subacute phase (peak prevalence occurs about 2–4 weeks after onset of disease; rarely appears after 6 weeks) and are at risk for coronary thrombosis acutely and coronary stenosis chronically. Carditis; aortic, mitral, and tricuspid regurgitation; pericardial effusion; CHF; MI; left ventricular dysfunction; and ECG changes may also occur.

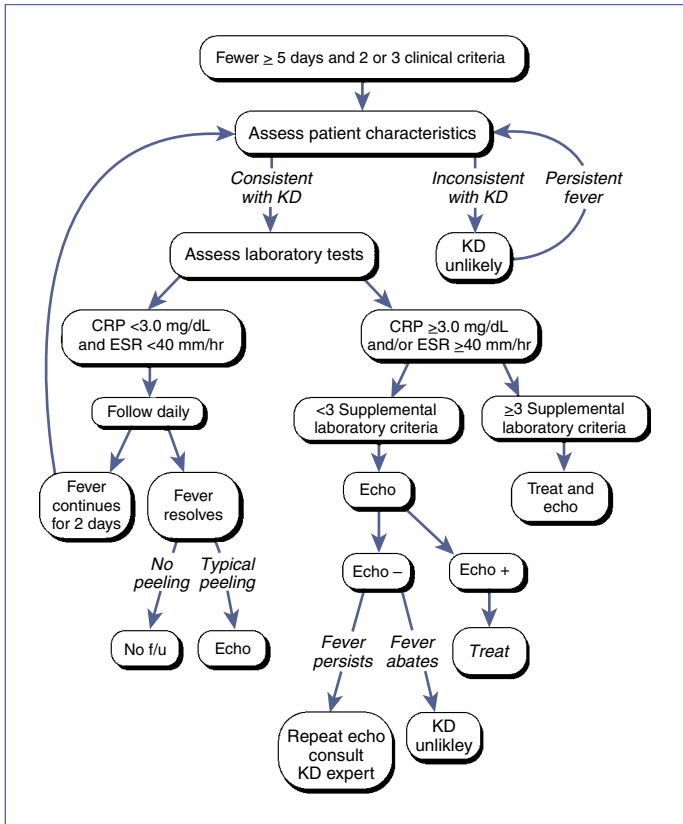


FIGURE 7-16

Evaluation of incomplete Kawasaki disease (KD). CRP, C-reactive protein; echo, echocardiogram; ESR, erythrocyte sedimentation rate; f/u, follow-up. (From Newburger JW, Takahashi M, Gerber MA, et al. *Diagnosis, treatment, and long term management of Kawasaki disease*. *Circulation*. 2004;110:2747-2771.)

6. **Convalescent phase:** ESR, CRP, and platelet count return to normal.

Those with coronary artery abnormalities are at increased risk for MI, arrhythmias, and sudden death.

7. **Management** (also see Table EC 7-C)<sup>16</sup>

a. Intravenous immunoglobulin (IVIG)

(1) Shown to reduce incidence of coronary artery dilation to <3% and decrease duration of fever if given in the first 10 days of illness. Current recommended regimen is a single dose of IVIG, 2 g/kg over 10–12 hours.



TABLE EC 7-C

## GUIDELINES FOR TREATMENT AND FOLLOW-UP OF CHILDREN WITH KAWASAKI DISEASE

Risk Level	Pharmacologic Therapy	Physical Activity	Follow-up and Diagnostic Testing	Invasive Testing
I: No coronary artery changes at any stage of illness	None beyond initial 6–8 weeks	No restrictions beyond initial 6–8 weeks	Counsel on cardiovascular risk factors every 5 years	None recommended
II: Transient coronary artery ectasia that resolves by 8 weeks after disease onset	None beyond initial 6–8 weeks	No restrictions beyond initial 6–8 weeks	Counsel on cardiovascular risk factors every 3–5 years	None recommended
III: Small to medium solitary coronary artery aneurysm	3–5 mg/kg/day aspirin, at least until aneurysm resolves	For patients in first decade of life, no restriction beyond initial 6–8 weeks; during second decade of life, physical activity guided by stress testing every 2 years; avoid competitive contact and high-impact sports while on antiplatelet therapy	Annual follow-up with echocardiogram and ECG	Angiography if stress testing or echocardiography suggests stenosis
IV: One or more large (>6 mm) aneurysms and coronary arteries with multiple small to medium aneurysms, without obstruction	Long-term aspirin (3–5 mg/kg/day) and warfarin or LMWH for patients with giant aneurysms	Annual stress testing guides physical activity; avoid competitive contact and high-impact sports while on anticoagulant therapy	Echocardiogram and ECG at 6-mo intervals, annual stress testing, atherosclerosis risk factor counseling at each visit	Cardiac catheterization 6–12 months after acute illness, with additional testing if ischemia noted or testing inconclusive
V: Coronary artery obstruction	Long-term aspirin (3–5 mg/kg/day); warfarin or LMWH if giant aneurysm persists; consider use of $\beta$ -blockers to reduce myocardial work	Contact sports, isometrics, and weight training should be avoided; other physical activity recommendations guided by outcome of stress testing or myocardial perfusion scan	Echocardiogram and ECG at 6-mo intervals, annual Holter and stress testing	Cardiac catheterization 6–12 months after acute illness to aid in selecting therapeutic options, additional testing if ischemia noted

LMWH, Low molecular weight heparin.

- (2) Some 10% of patients treated with IVIG fail to respond (persistent or recurrent fever  $\geq 36$  hr after IVIG completion). Re-treat with second dose.
- b. Aspirin is recommended for both its antiinflammatory and antiplatelet effects. American Heart Association (AHA) recommends initial high-dose aspirin (80–100 mg/kg/day divided in four doses) until 48–72 hours after defervescence. Given with IVIG. Then continue with low-dose aspirin (3–5 mg/kg/day as a single daily dose) for 6–8 weeks or until platelet count and ESR are normal (if there are no coronary artery abnormalities) or indefinitely if coronary artery abnormalities persist.
- c. Dipyridamole, 4 mg/kg divided in three doses, is sometimes used as an alternative to aspirin, particularly if symptoms of influenza or varicella arise while on aspirin (concern for Reye syndrome).
- d. Follow-up: Serial echocardiography is recommended to assess coronary arteries and left ventricular function (at time of diagnosis, at 2 weeks, at 6–8 weeks, and at 12 months [optional]). More frequent intervals and long-term follow-up are recommended if abnormalities are seen on echocardiography. Cardiac catheterization may be necessary.

### F. Rheumatic Heart Disease

1. **Etiology:** Believed to be immunologically mediated delayed sequela of group A streptococcal pharyngitis
2. **Clinical findings:** History of streptococcal pharyngitis 1–5 weeks before onset of symptoms. Often with pallor, malaise, easy fatigability.
3. **Diagnosis:** Jones criteria ([Box 7-5](#))
4. **Management:** Penicillin, bed rest, salicylates, supportive management of CHF (if present) with diuretics, digoxin, morphine

### G. Lyme Disease

1. **Etiology:** Following infection with *Borrelia burgdorferi*
2. **Clinical symptoms:** About 8%–10% of patients will get AV block. Other possible cardiac symptoms include myocarditis and pericarditis.

## VIII. EXERCISE RECOMMENDATIONS FOR CONGENITAL HEART DISEASE

See [Table EC 7-D](#) for exercise recommendations for congenital heart disease.<sup>17</sup>

## IX. LIPID MONITORING RECOMMENDATIONS

### A. Screening of Children and Adolescents<sup>18</sup>

1. **Universal screening** of non-fasting non-HDL cholesterol in children 9–11 years old (prior to onset of puberty) and again in individuals 17–21 years
2. **Targeted screening** should occur in children 2–8 years old and adolescents 12–16 years old, with two fasting lipid profiles (between 2 weeks and 3 months apart, results averaged) for the following risk factors:
  - a. Moderate or high-risk medical condition (history of prematurity, VLBW, congenital heart disease (repaired or nonrepaired), recurrent urinary

TABLE EC 7-D

**EXERCISE RECOMMENDATIONS FOR CONGENITAL HEART DISEASE AND SPORTS ALLOWED FOR SOME SPECIFIC CARDIAC LESIONS<sup>15</sup>**

Diagnosis	Sports Allowed		
Small ASD or VSD	All		
Mild aortic stenosis	All		
MVP (without other risk factors)	All		
Moderate aortic stenosis	IA, IB, IIA		
Mild LV dysfunction	IA, IB, IC		
Moderate LV dysfunction	IA only		
Long QT syndrome	IA only		
Hypertrophic cardiomyopathy	None (or IA only)		
Severe aortic stenosis	None		

Sports Classification	Low Dynamic (A)	Moderate Dynamic (B)	High Dynamic (C)
I. Low static	Billiards Bowling Golf Riflery	Baseball/softball Table tennis Volleyball Fencing	Racket sports Cross-country skiing Field hockey* Race walking Running (long distance) Soccer*
II. Moderate static	Archery Auto racing*,† Diving*,† Equestrian*,† Motorcycling*,†	Fencing Field events (jumping) Figure skating* Football (American)* Surfing Rugby* Running (sprint) Synchronized swim†	Basketball* Ice hockey* Cross-country skiing (skating technique) Swimming Lacrosse* Running (middle distance) Team handball
III. High static	Bobsledding Field events Gymnastics*,† Rock climbing Sailing Windsurfing*,† Waterskiing*,† Weight lifting*,†	Body building*,† Downhill skiing*,† Skateboarding*,†	Boxing/wrestling* Martial arts* Rowing Speed skating Cycling*,†

\*Danger of bodily collision.

†Increased risk if syncope occurs.

ASD, Atrial septal defect; LV, left ventricular; MVP, mitral valve prolapse; VSD, ventricular septal defect.

Adapted from Maron BJ, Zipes DP. 36th Bethesda Conference: Eligibility recommendations for competitive athletes with cardiovascular abnormalities. *J Am Coll Cardiol.* 2005;45:1313-1375; and Committee on Sports Medicine and Fitness, American Academy of Pediatrics. Medical conditions affecting sports participation. *Pediatrics.* 2001;107:1205-1209.

## BOX 7-5

**GUIDELINES FOR DIAGNOSIS OF INITIAL ATTACK OF RHEUMATIC FEVER (JONES CRITERIA)**

Major Manifestations	Minor Manifestations
Carditis	Clinical findings:
Polyarthrititis	Arthralgia
Chorea	Fever
Erythema marginatum	Laboratory findings:
Subcutaneous nodule	Elevated acute phase reactants (erythrocyte sedimentation rate, C-reactive protein)
	Prolonged PR interval

**Plus****Supporting evidence of antecedent group A streptococcal infection**

Positive throat culture or rapid streptococcal antigen test

Elevated or rising streptococcal antibody titer

**NOTE:** If supported by evidence of preceding group A streptococcal infection, the presence of two major manifestations or of one major and two minor manifestations indicates a high probability of acute rheumatic fever.

tract infections, known renal or urologic malformations, family history of congenital renal disease, solid organ transplant, malignancy or bone marrow transplant, treatment with drugs known to raise blood pressure, other systemic illness associated with hypertension (neurofibromatosis, tuberous sclerosis), evidence of elevated intracranial pressure

- b. Have other cardiovascular risk factors (diabetes, hypertension, body mass index [BMI]  $\geq$  95th percentile, smoke cigarettes)
- c. Have a family history of early cardiovascular disease (CVD) or severe hypercholesterolemia
  - (1) Parent or grandparent who is < 55 years old (males) or < 65 years old (females) and had suffered a myocardial infarction or sudden death, undergone a coronary artery procedure, or who otherwise had evidence of coronary atherosclerosis, peripheral vascular disease, or cerebrovascular disease
  - (2) Parent with total cholesterol  $\geq$  240 mg/dL or known dyslipidemia

**B. Goals for Lipid Levels in Childhood****1. Total cholesterol**

- a. Acceptable (<170 mg/dL): Repeat measurement in 3–5 years
- b. Borderline (170–199 mg/dL): Repeat cholesterol and average with previous measurement. If <170, repeat in 3–5 years. If  $\geq$ 170, obtain lipoprotein analysis.
- c. High ( $\geq$ 200 mg/dL): Obtain lipoprotein analysis

**2. Low-density lipoprotein (LDL) cholesterol**

- a. Acceptable (<110 mg/dL)
- b. Borderline (110–129 mg/dL)
- c. High ( $\geq$ 130 mg/dL)

### C. Management of Hyperlipidemia<sup>18</sup>

1. **Normal and borderline elevated LDL levels:** Education, risk factor intervention including diet, smoking cessation, and an exercise program. For borderline levels, reevaluate in 1 year.
2. **High LDL levels:** Examine for secondary causes (liver, thyroid, renal disorders) and familial disorders. Initiate low-fat, low-cholesterol diet; reevaluate in 6 months. **Note:** For LDL cholesterol > 250 or triglyceridemia >500, refer directly to a lipid specialist.
3. **Drug therapy:** Should be considered in children >10 years of age after failure of 6- to 12-month trial of diet therapy as follows:
  - a. LDL >190mg/dL without other cardiovascular disease risk factors
  - b. LDL >160mg/dL with risk factors (diabetes, obesity, hypertension, positive family history of premature CVD)
  - c. LDL >130mg/dL in children with diabetes mellitus
  - d. Bile acid sequestrants and statins are the usual first-line drugs for treatment in children.
4. **Persistently high triglycerides (>150 mg/dL) and reduced HDL (<35 mg/dL):** Evaluate for secondary causes (diabetes, alcohol abuse, renal or thyroid disease). Treatment is diet and exercise.

## X. CARDIOVASCULAR SCREENING

### A. Sports<sup>19</sup>

There is no established mandated preparticipation sports screening. There is a recommended history and physical examination screening from the American Heart Association (AHA). Routine ECGs are not required unless there is suspicion of underlying cardiac disease (Box EC 7-A).

### B. Attention Deficit/Hyperactivity Disorder (ADHD)

1. **Obtain a good patient and family history as well as physical examination.**
2. **There is not an increased risk of sudden cardiac death** in children without cardiac disease taking ADHD medications. There is no consensus on universal ECG screening. ECGs should be obtained in those who screen with positive answers on history, polypharmacy, tachycardia while on medications, and history of significant cardiac disease. If a patient has significant heart disease or concern for cardiac disease, have patient evaluated by a pediatric cardiologist.

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**BOX EC 7-A****THE 12-ELEMENT AMERICAN HEART ASSOCIATION (AHA) RECOMMENDATIONS FOR PARTICIPATION CARDIOVASCULAR SCREENING OF COMPETITIVE ATHLETES****Medical History\*****Personal History**

1. Exertional chest pain/discomfort
2. Unexplained syncope/near syncope<sup>†</sup>
3. Excessive exertional and unexplained dyspnea/fatigue associated with exercise
4. Prior recognition of a heart murmur
5. Elevated systemic blood pressure

**FAMILY HISTORY**

1. Premature death (sudden and unexpected or otherwise) before age 50 years due to heart disease, in  $\geq 1$  relative
2. Disability from heart disease in a close relative <50 years of age
3. Specific knowledge of certain cardiac conditions in family members: hypertrophic or dilated cardiomyopathy, long-QT syndrome or other ion channelopathies, Marfan syndrome, or clinically important arrhythmias

**PHYSICAL EXAMINATION**

1. Heart murmur<sup>‡</sup>
2. Femoral pulses to exclude aortic coarctation
3. Physical stigmata of Marfan syndrome
4. Brachial artery blood pressure (sitting position)<sup>§</sup>

\*Parental verification is recommended for high school and middle school athletes.

<sup>†</sup>Judged not to be neurocardiogenic (vasovagal); of particular concern when related to exertion.

<sup>‡</sup>Auscultation should be performed in both supine and standing positions (or with Valsalva maneuver), specifically to identify murmurs of dynamic left ventricular outflow tract obstruction.

<sup>§</sup>Preferably taken in both arms.

From Maron BJ, Thompson PD, Ackerman MJ, et al. Recommendations and considerations related to preparticipation screening for cardiovascular abnormalities in competitive athletes: 2007 update: a scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism: endorsed by the American College of Cardiology Foundation. *Circulation*. 2007;115:1643-1655.

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# Chapter 8

## Dermatology

Jing Fang, MD

### I. WEBSITE

Dermatology Image Atlas: <http://www.dermatlas.org>

**NOTE:** Please refer to the color plates in this chapter for photographic examples of dermatologic findings.

### II. EVALUATION AND CLINICAL DESCRIPTIONS OF SKIN FINDINGS

#### A. Primary Skin Lesions (Fig. 8-1)

1. **Macule:** Small flat lesion with altered color (<1 cm)
2. **Patch:** Large macule (>1 cm), also used to describe large macule with scale
3. **Papule:** Elevated, well-circumscribed lesion (<1 cm)
4. **Plaques:** Large papule (>1 cm)
5. **Nodule:** Mass located in dermis or subcutaneous fat (may be solid or soft)
6. **Tumor:** Large nodule
7. **Vesicle:** Blister with transparent fluid
8. **Bulla:** Large vesicle
9. **Wheal:** Erythematous, well-circumscribed, raised, edematous lesion that appears and disappears quickly

#### B. Secondary Skin Lesions (see Fig. 8-1)

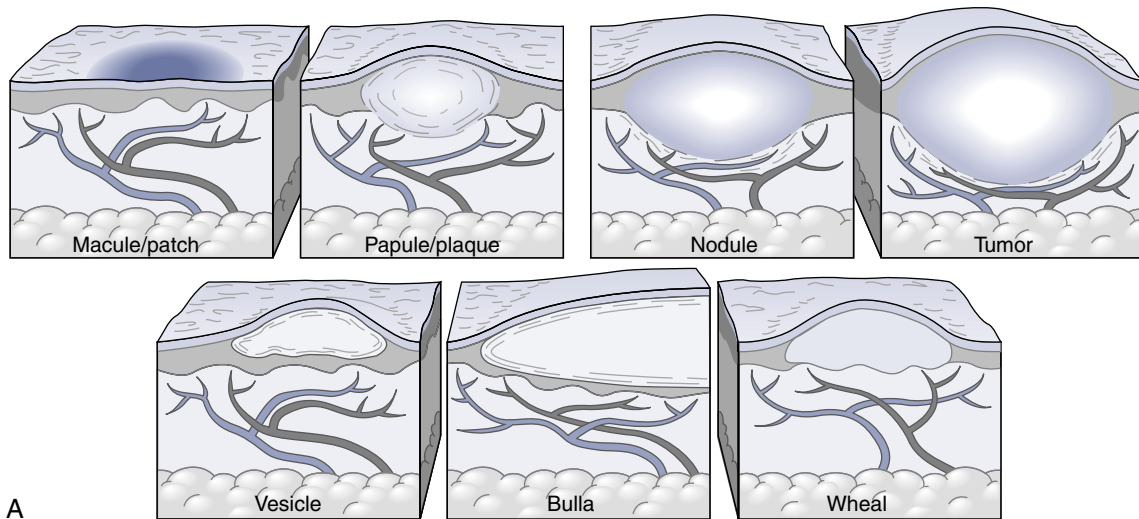
1. **Scale:** Small, thin plate of horny epithelium
2. **Pustule:** Well-circumscribed elevated lesion filled with pus
3. **Crust:** Exudative mass consisting of blood, scale, and pus from skin erosions or ruptured vesicles/papules
4. **Ulcer:** Erosion of dermis and cutis, with clearly defined edges
5. **Scar:** Formation of new connective tissue after damage to epidermis and cutis, leaving permanent change in skin
6. **Excoriation:** Surface marks, often linear secondary to scratching
7. **Fissure:** Linear skin crack with inflammation and pain

### III. SKIN LUMPS: DIAGNOSIS AND TREATMENT (FIGS. 8-2 TO 8-13)

#### A. Hemangiomas (Fig. 8-2, color)

1. **Pathogenesis:** Benign vascular tumor of infancy, with a phase of rapid proliferation (densely packed endothelial cells form small capillaries, and subsequent vessels develop from existing vasculature), followed by phase of spontaneous involution.
2. **Clinical presentation:**
  - a. Not fully formed at birth. Some newborns may demonstrate pale macules with threadlike telangiectasias that later develop into hemangiomas.



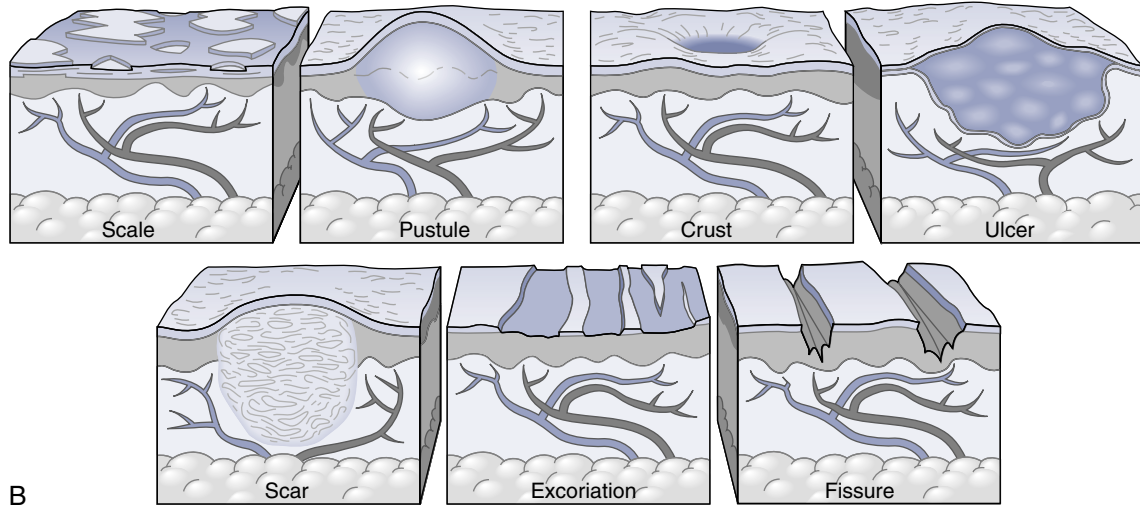


A

FIGURE 8-1

Pattern diagnosis. A, Primary skin lesions.

Continued



**FIGURE 8-1, cont'd**

**B,** Secondary skin lesions. (From Cohen BA. *Pediatric Dermatology*. 2nd ed. St Louis: Mosby, 1999:5.)

- b. Superficial usually noted first, but most with both superficial and deep components.
  - (1) Superficial: Bright red papule, nodule, plaque
  - (2) Deep: Firm, rubbery nodule/tumor, often with overlying blue-purple discoloration
- c. Size: Range from a few millimeters to many centimeters.
- d. After involution, can have residual skin changes, including scarring and atrophy.
- 3. **Incidence:** Most common tumor of infancy. Low birth weight highest risk factor; increased risk in Caucasian infants (5%–10%, less common in other ethnic groups), premature infants, and females.
- 4. **Natural history:** Most occur within 2 days to 2 months of life. Undergo rapid growth phase in first few months, with 80% peaking by 3 months. Many begin to regress by 6 months, with rate of 10% complete involution per year (i.e., 50% or more completely involuted by 5 years).
- 5. **Diagnosis:** Usually diagnosed clinically. Atypical clinical findings, growth pattern, and equivocal imaging should prompt tissue biopsy to exclude other neoplasms or unusual vascular malformations.
- 6. **Complications:**
  - a. Ulceration: Most common complication. Can be extremely painful and will scar. Can also bleed and become superinfected.
  - b. Bleeding: Usually minimal, can be stopped with direct pressure.
  - c. Visual obstruction: From periorbital hemangiomas, especially involving upper medial eyelid. Require evaluation by an ophthalmologist.
  - d. Airway obstruction: Seen with airway hemangiomas. Infants with lesions in a beard distribution (i.e., chin, lower lip, mandible, anterior neck) are at greater risk. May have hoarseness, stridor, cough, and cyanosis.
  - e. Otitis externa: From ear hemangiomas that obstruct the auditory canal.
  - f. Deformation/destruction of important cosmetic structures: From especially large lesions (i.e., ear, nasal septum, vermillion border).
  - g. Rare complications:
    - (1) Kasabach-Merritt phenomenon: Associated with hemangiopericytomas, tufted angiomas, or kaposiform hemangioendotheliomas, not true infantile hemangiomas. Rare complication due to platelet trapping within rapidly growing vascular tumor. Characterized by severe thrombocytopenia, coagulopathy, and variable degree of hemolytic anemia. Differentiated from benign hemangiomas by their deep red-blue appearance, marked firmness, and histologic appearance.
    - (2) PHACES syndrome: **P**osterior cranial fossa malformations (as well as multiple other cerebral arteriovenous anomalies), large segmental facial **H**emangiomas, **A**rterial lesions, **C**ardiac abnormalities (aortic coarctation, other anomalies of the aortic and mesenteric vessels), **E**ye abnormalities, **S**ternal cleft anomalies/supraumbilical raphes.<sup>1</sup>
    - (3) Visceral hemangiomas: Usually hepatic hemangiomas; most are asymptomatic and can be observed without imaging. Rarely, can cause massive hepatosplenomegaly and heart failure. Associated

with segmental hemangiomas and multiple cutaneous hemangiomas, although may be isolated lesions.

- (4) Sacral syndrome: Tethered cord, spinal, anorectal, and urogenital anomalies, associated with lumbosacral hemangiomas. Require evaluation with magnetic resonance imaging (MRI).

## 7. Management:

- a. Most require no intervention. Decision to treat should be based on location, size, pattern, age of patient, and risk of complications. Photo documentation is used to follow the growth and regression process.
- b. Treatment of clinically significant infantile hemangiomas<sup>2</sup>:
- (1) Propranolol:
- (a) Considered an off-label use. There is no U.S. Food and Drug Administration (FDA)-approved medical treatment for infantile hemangiomas, but propranolol is now accepted by pediatric dermatologists as the standard of care. Should be initiated under careful supervision of a pediatric dermatologist or other practitioner experienced in management.
- (b) Patients should be clinically screened for cardiac disease. Electrocardiogram (ECG) and/or echocardiogram are not required but obtained only when indicated (e.g., heart murmur, suspected cardiac/other vascular anomalies).
- (c) Inpatient treatment: Infants < 2 months or those deemed at risk for complications from oral propranolol should be admitted for 48 hours for initiation of therapy.
- (i) Goal dosing: 2 mg/kg/day. Recommend starting with 1 mg/kg/day divided TID for 24 hours, then increasing to 2 mg/kg/day divided TID for 24 hours.  
Side effects: Bradycardia, hypotension, hypoglycemia. Blood pressure and heart rate should be monitored 1 hour after each dose. Blood glucose should be checked as indicated for unexpected changes in behavior (e.g., jitteriness, somnolence).
- (ii) Child can be discharged if six doses of medication are tolerated without complications. Pediatrician should be notified at time of discharge.
- (d) Outpatient treatment: Healthy infants >2 months can start therapy in a supervised clinic setting. Initial clinic visit should be 2 hours long.
- (i) Goal dosing: 2 mg/kg/day. Give initial dose in clinic. Recommend starting with 1 mg/kg/day divided TID for 5 days, then increase to 1.5 mg/kg/day divided TID for another 5 days, and finally after day 10, increase to 2 mg/kg/day divided TID. Vital signs should be monitored before starting first dose, then Q30 min until discharge from clinic. Parents should be trained during visit to check heart rate and assess for signs of hypoglycemia.

- (e) Average length of treatment is 6–9 months. Most patients can be tapered from propranolol at their first birthday; tapering can be monitored over 10–14 days. Younger infants tend to have a longer treatment course owing to higher rates of rebounds. Significant rebound should be treated by restarting medication.
- (2) Steroids: No randomized trials to compare propranolol and systemic oral corticosteroids, but retrospective data suggest propranolol is more effective and has fewer adverse effects.
- (3) Topical timolol: Efficacy noted in superficial hemangiomas and treatment duration > 3 months.

## B. Warts

1. **Pathogenesis:** Caused by more than 100 types of human papillomavirus (HPV). Spread by skin-to-skin contact.
2. **Clinical presentation:**
  - a. Common warts: Skin-colored, rough, minimally scaly papules and nodules found most commonly on the hands, although can occur anywhere on the body. Can be solitary or multiple, range from a few millimeters to several centimeters, and may form large plaques or a confluent linear pattern secondary to autoinoculation. May be persistent in immunocompromised patients.
  - b. Flat warts: Occur over the hands, arms, and face; usually <2 mm wide. Often present in clusters.
  - c. Plantar warts: Occur on soles of feet. Can be painful; appear as inward-growing, hyperkeratotic plaques and papules. Trauma on weight-bearing surfaces results in small black dots (petechiae from thrombosed vessels on the surface of the wart).
  - d. Anogenital warts: See Chapter 5.
3. **Management<sup>3</sup>:**
  - a. Spontaneous resolution occurs in >75% of warts in otherwise healthy individuals within 3 years. No treatment clearly better than placebo, except for topical salicylic acid.
  - b. Keratolytics (i.e., topical salicylates): Work by removing excess scale within and around warts and by triggering an inflammatory reaction. Particularly effective in combination with adhesive tape occlusion; response may take 4–6 months.
  - c. Destructive techniques: Not more effective than placebo. Can be painful and cause scarring, so not recommended in children.

## C. Molluscum Contagiosum (Fig. 8-3, color)

1. **Pathogenesis:** Caused by large DNA poxvirus. Spread by skin-to-skin contact.
2. **Clinical presentation:** Dome-shaped, often umbilicated, translucent to white papules that range from 1 mm to 1 cm. May be pruritic and can be surrounded with erythema, resembling eczema. Can occur anywhere except palms and soles, most commonly on the trunk and intertriginous

areas. Can occur in the genital area and lower abdomen when obtained as a sexually transmitted infection.

3. **Management:** Most spontaneously resolve within a few months and do not require intervention. Treatment may cause scarring and not more effective than placebo. Recurrences common. Monitor for secondary bacterial infection.

#### **D. Pyogenic Granuloma (Lobular Capillary Hemangioma) (Fig. 8-4, color)**

1. **Clinical presentation:** Benign vascular tumor, appears as small bright red papule that grows over several weeks to months into sessile or pedunculated papule with a "collarette" or scale. Usually no bigger than 1 cm. Can bleed profusely with minor trauma and can ulcerate. Rarely spontaneously regresses. Seen in all ages; average age of diagnosis 6 months to 10 years. Located on head and neck, sometimes in oral mucosa.
2. **Management:** Treatment usually required, given frequent bleeding and ulceration.
  - a. Shave excision or curettage with cautery of base: Recommended for pedunculated lesions.
  - b. Surgical excision: May be necessary for large or unusual lesions, but recurrence rates are high.
  - c. Laser therapy: Can be used for small pyogenic granulomas but may require 2 to 3 treatments.

#### **E. Scabies (Fig. 8-5, color)**

1. **Pathogenesis:** Caused by the mite *Sarcoptes scabiei*. Spread by skin-to-skin contact and through fomites; can live for 2 days away from a human host. Female mites burrow under the skin at a rate of 2 mm/day and lay eggs as they tunnel (up to 25 eggs).
2. **Clinical presentation:** Initial lesion is a small, erythematous papule that is easy to overlook. Can have burrows (elongated, edematous papulovesicles, often with a pustule at the advancing border), which are pathognomonic. Most commonly located in interdigital webs, wrist folds, elbows, axilla, buttocks, and belt line. Burrows are most dramatic in patients who are unable to scratch (e.g., infants). Disseminated eczematous eruption results in generalized severe pruritus, especially at night. Can become nodular, particularly in intertriginous areas, or be susceptible to superinfection due to frequent excoriations.
3. **Treatment<sup>4</sup>:**
  - a. Permethrin cream: 5% cream applied to affected areas of skin, including under fingernails, face, and scalp. Rinse off after 8–14 hours. Can repeat in 7–10 days.
  - b. Ivermectin (off-label use): 200 mcg/kg oral dose; can repeat in 2 weeks. Efficacy comparable to permethrin cream.

#### **F. Reactive Erythema (Figs. 8-6 to 8-13)**

1. **Clinical presentation:** Group of disorders characterized by erythematous patches, plaques, and nodules that vary in size, shape, and distribution.
2. **Etiology:** Represent cutaneous reaction patterns triggered by endogenous and environmental factors.

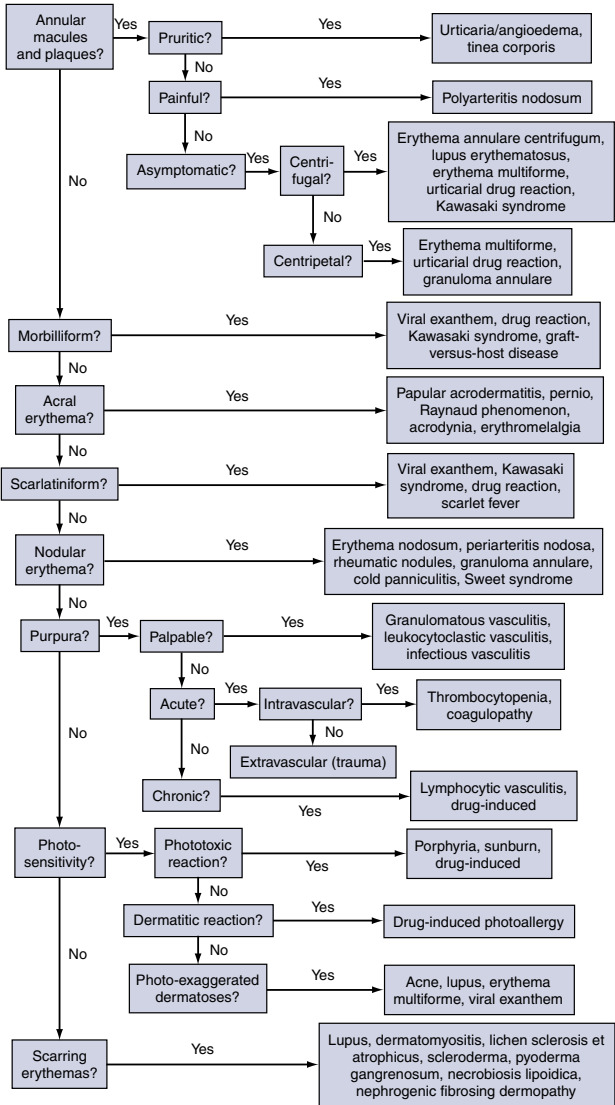


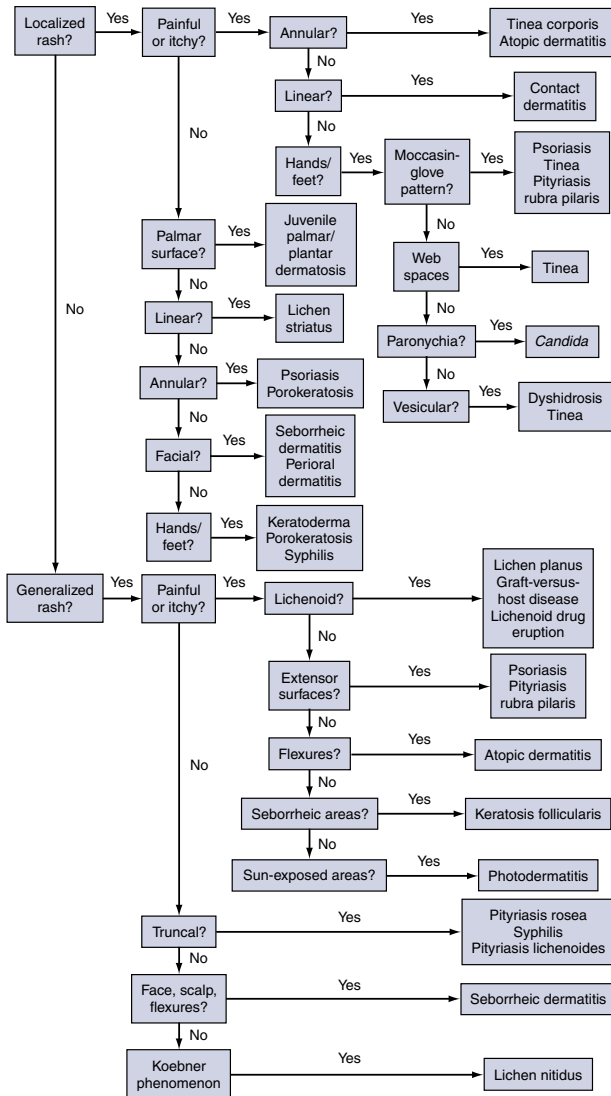
FIGURE 8-6

Reactive erythema. (Modified from Cohen BA. Atlas of Pediatric Dermatology. 3rd ed. St Louis: Mosby, 2005:196.)

**IV. PAPULOSQUAMOUS LESIONS: DIAGNOSIS AND TREATMENT****(FIGS. 8-14 TO 8-25)****A. Atopic Dermatitis (Eczema) (Figs. 8-22 to 8-26, color)**

1. **Pathogenesis:** Due to impaired skin barrier function from combination of genetic and environmental factors, including a defect in filaggrin, a protein essential for keratinization and epidermal homeostasis. An inadequate skin barrier leads to transepidermal water loss. Can be associated with elevated serum immunoglobulin (Ig)E.
2. **Epidemiology:** Affects up to 20% of children in the United States, the vast majority with onset before 5 years. Many with other comorbidities including asthma, allergic rhinitis, and food allergies. Eczema resolves or improves in over 75% of patients by adulthood.
3. **Clinical presentation:** Dry, pruritic skin with acute changes including erythema, vesicles, crusting, and chronic changes, including lichenification, scaling, and postinflammatory hypopigmentation or hyperpigmentation.
  - a. Infantile form: Erythematous, scaly lesions on the cheeks, scalp, and extensor surfaces. Diaper area usually spared.
  - b. Childhood form: Lichenified plaques in flexural areas.
  - c. Adolescence: More localized and lichenified skin changes. May be predominantly on hands and feet.
4. **Treatment<sup>5</sup>:**
  - a. Lifestyle: Avoiding triggers, including products with alcohol, fragrances, and astringents, sweat, allergens, and excessive bathing. Bathing time should be <5 minutes, skin should be patted dry (not rubbed) afterward and followed by rapid application of an emollient.
  - b. Skin hydration: Frequent use of bland lubricants with low or no water content (e.g., petroleum jelly, Vaseline, Aquaphor). Lotions have high water and low oil content and can actually worsen dry skin.
  - c. Antihistamines: Used primarily for sedating effects. Also helpful in children with concomitant environmental allergies or hives.
  - d. Treatment for inflammation:
    - (1) Topical steroids ([Table 8-1](#)):
      - (a) Low- and medium-potency steroid ointments once or twice daily for 7 days for eczema flares. Severe flares may require a higher-potency steroid for a longer duration of therapy, followed by a taper to lower-potency steroids. Use of topical steroids in areas where skin is thin (i.e., groin, axilla, face, under breasts) should generally be avoided, although can consider short duration of low-potency steroid for these areas. Topical lubricant can be applied over steroid.
    - (2) Topical calcineurin inhibitors: Tacrolimus ointment, pimecrolimus cream
      - (a) Second-line therapy; should be used in consultation with a dermatologist. In 2006, the FDA placed a "black box" warning on these medications because of possible increased risk of cancer, although no data confirm this as yet, and long-term safety studies are pending.<sup>6</sup>



**FIGURE 8-14**

Papulosquamous disorders algorithm. (Modified from Cohen BA. Atlas of Pediatric Dermatology. 3rd ed. St Louis: Mosby, 2005:97.)

TABLE 8-1

## TOPICAL STEROID POTENCY RANKING

Brand Name	Generic Name
<b>CLASS 1—SUPERPOTENT</b>	
Clobex Lt/Spray/Shampoo, 0.05%	Clobetasol propionate
Cormax Cr/Sol, 0.05%	Clobetasol propionate
Diprolene Ot, 0.05%	Betamethasone dipropionate
Olux E Foam, 0.05%	Clobetasol propionate
Olux Foam, 0.05%	Clobetasol propionate
Temovate Cr/Ot/Sol, 0.05%	Clobetasol propionate
Ultravate Cr/Ot, 0.05%	Halobetasol propionate
Vanos Cr, 0.1%	Fluocinonide
Psorcon Ot, 0.05%	Difflorasone diacetate
Psorcon E Ot, 0.05%	Difflorasone diacetate
<b>CLASS 2—POTENT</b>	
Diprolene Cr AF, 0.05%	Betamethasone dipropionate
Elocon Ot, 0.1%	Mometasone furoate
Florone Ot, 0.05%	Difflorasone diacetate
Halog Ot/Cr, 0.1%	Halcinonide
Lidex Cr/Gel/Ot, 0.05%	Fluocinonide
Psorcon Cr, 0.05%	Difflorasone diacetate
Topicort Cr/Ot, 0.25%	Desoximetasone
Topicort Gel, 0.05%	Desoximetasone
<b>CLASS 3—UPPER MID-STRENGTH</b>	
Cutivate Ot, 0.005%	Fluticasone propionate
Lidex-E Cr, 0.05%	Fluocinonide
Luxiq Foam, 0.12%	Betamethasone valerate
Topicort LP Cr, 0.05%	Desoximetasone
<b>CLASS 4—MID-STRENGTH</b>	
Cordran Ot, 0.05%	Flurandrenolide
Elocon Cr, 0.1%	Mometasone furoate
Kenalog Cr/Spray, 0.1%	Triamcinolone acetonide
Synalar Ot, 0.03%	Flucinolone acetonide
Westcort Ot, 0.2%	Hydrocortisone valerate
<b>CLASS 5—LOWER MID-STRENGTH</b>	
Capex Shampoo, 0.01%	Fluocinolone acetonide
Cordran Cr/Lt/Tape, 0.05%	Flurandrenolide
Cutivate Cr/Lt, 0.05%	Fluticasone propionate
Derm Atop Cr, 0.1%	Prednicarbate
Des Owen Lt, 0.05%	Desonide
Locoid Cr/Lt/Ot/Sol, 0.1%	Hydrocortisone
Pandel Cr, 0.1%	Hydrocortisone
Synalar Cr, 0.03%/0.01%	Flucinolone acetonide
Westcort Cr, 0.2%	Hydrocortisone valerate
<b>CLASS 6—MILD</b>	
Aclovate Cr/Ot, 0.05%	Alclometasone dipropionate
Derma-Smoother/FS Oil, 0.01%	Fluocinolone acetonide
Desonate Gel, 0.05%	Desonide
Synalar Cr/Sol, 0.01%	Fluocinolone acetonide
Verdeso Foam, 0.05%	Desonide

TABLE 8-1

## TOPICAL STEROID POTENCY RANKING (Continued)

Brand Name	Generic Name
<b>CLASS 7—LEAST POTENT</b>	
Cetacort Lt, 0.5%/1%	Hydrocortisone
Cortaid Cr/Spray/Ot	Hydrocortisone
Hytone Cr/Lt, 1%/2.5%	Hydrocortisone
Micort-HC Cr, 2%/2.5%	Hydrocortisone
Nutracort Lt, 1%/2.5%	Hydrocortisone
Synacort Cr, 1%/2.5%	Hydrocortisone

National Psoriasis Foundation: Available at [http://www.psoriasis.org/netcommunity/sublearn03\\_mild\\_potency](http://www.psoriasis.org/netcommunity/sublearn03_mild_potency). Accessed August 16, 2010.

### 5. Complications<sup>7</sup>:

- Bacterial superinfection: Usually *Staphylococcus aureus*, sometimes group A *Streptococcus*. Depending on extent of infection, can be treated with topical mupirocin to systemic antibiotics. Can also take diluted bleach baths once to twice a week (mix 1/4 to 1/2 cup of bleach in full tub of lukewarm water and soak for 10 minutes, then rinse off with fresh water).
- Eczema herpeticum superinfection with herpes simplex virus 1 (HSV-1) or -2, can cause severe systemic infection. Presents as vesiculopustular lesions with central punched-out erosions that do not respond to oral antibiotics. Must be treated systemically with acyclovir/valacyclovir. Should be evaluated by ophthalmologist if there is concern for eye involvement.

### B. Papular Urticaria (Fig. 8-27, color)

- Pathogenesis:** Caused by insect bite-induced hypersensitivity (IBIH), usually from fleas, mosquitos, or bedbugs. Due to delayed type IV hypersensitivity reactions.

- Clinical presentation/epidemiology:** Summarized by the SCRATCH principles<sup>8</sup>:

**Symmetric eruption:** Exposed areas and scalp commonly affected. Sparing diaper region, palms, and soles.

**Cluster:** Appear as "meal clusters" or "breakfast, lunch, dinner," which are linear or triangular groupings of lesions. Associated with bedbugs and fleas.

**Rover not required:** A remote animal exposure or lack of pet at home does not rule out IBIH.

**Age:** Tends to peak by 2 years of age. Not seen in newborn period. Most tend to develop tolerance by age 10.

**Target lesions:** Characteristic of IBIH, especially in more darkly pigmented patients. Also, **Time:** emphasize chronic nature of eruption and need for patience and watchful waiting.

**Confused pediatrician/parent:** Diagnosis often met with disbelief by parent and/or referring pediatrician.

**Household:** Because of the nature of hypersensitivity, usually only affects one family member in the household.

### 3. Management (the 3 Ps):

**Prevention:** Wear protective clothing, use insect repellent when outside, launder bedding and mattress pads for bedbugs, and maximize flea control for pets.

**Pruritus control:** Topical steroids or antihistamines may be of some benefit.

**Patience:** IBIH can be frustrating because of its persistent, recurrent nature. Ensure patients that their symptoms will resolve and they will eventually develop tolerance.

### C. Ichthyosis (Fig. 8-28, color)

1. **Pathogenesis:** Diverse group of hereditary skin disorders of keratinization defects. Includes congenital ichthyosiform erythroderma, lamellar ichthyosis, epidermolytic ichthyosis, ichthyosis vulgaris, harlequin ichthyosis, and X-linked ichthyosis.
2. **Management:** Symptoms can be asymptomatic/mild to life-threatening. Basic management is aggressive skin hydration with emollients. Refer to dermatologist if therapy does not work, diagnosis is unclear, or there are other complications. Genetic markers available for many variants.

### D. Tinea Versicolor (Fig. 8-29, color)

1. **Pathogenesis:** Caused by *Malassezia* (previously *Pityrosporum*), a lipid-dependent yeast. Exacerbated by hot/humid weather, hyperhidrosis, topical skin oil use. Not associated with poor hygiene. Not contagious.
2. **Clinical presentation:** Macules or patches that are hypopigmented, hyperpigmented, or erythematous. Hypopigmented areas tend to be more prominent in the summer because affected areas do not tan. Lesions often have a fine scale and can be mildly pruritic but are usually asymptomatic.
3. **Diagnosis:** Potassium hydroxide (KOH) microscopy reveals hyphae and yeast cells that appear like "spaghetti and meatballs."
4. **Treatment:** Topical antifungals (miconazole, oxiconazole, ketoconazole) or selenium sulfide are effective. Given the risk of hepatotoxicity, oral azole antifungals are reserved for resistant or widespread disease (oral terbinafine not effective). Pigmentation changes may take months to resolve despite successful treatment.

### E. Tinea Corporis<sup>9</sup>

1. **Pathogenesis:** Caused by *Trichophyton* (anthropophilic) and *Microsporum* (zoophilic) species. Other species rarely involved. Can be spread through direct contact and fomites, especially in sports where there is close contact (e.g., wrestling).
2. **Clinical presentation:** Pruritic, erythematous, annular patch or plaque with central clearing and a scaly raised border. Typically affects glabrous skin (smooth and bare).
3. **Diagnosis:** Usually diagnosed clinically, but a KOH preparation or fungal culture can be used to help guide diagnosis.
4. **Treatment:** Topical antifungals (terbinafine, azole antifungals) until the lesion resolves, plus 1–2 additional weeks. Widespread eruption may require oral antibiotics.

## V. HAIR LOSS: DIAGNOSIS AND TREATMENT (FIGS. 8-30 TO 8-34)

## A. Tinea Capitis (Fig. 8-30, color)

1. **Pathogenesis:** Mostly caused by *Trichophyton tonsurans* (but *Trichophyton violaceum* and *Trichophyton sudanense* clinically similar); sometimes *Microsporum canis*. Can be spread through contact and fomites.
2. **Epidemiology:** Usually occurs in young children, 1–10 years of age. African-American children more commonly affected, perhaps owing to the structure of their hair, but any age and any ethnicity can be affected.
3. **Clinical presentation:**
  - a. Black dot tinea capitis: Most common. Slowly growing, erythematous, scaling patches. These areas develop alopecia, and black dots are visible on scalp where hair has broken off.
  - b. Gray patch ("seborrheic dermatitis") tinea capitis: Erythematous, scaling, well-demarcated patch that grows centrifugally. Hair breaks off a few millimeters above scalp and takes on a gray/frosted appearance.
  - c. Kerion (Fig. 8-31, color): Complication of tinea capitis or tinea corporis. Type IV delayed hypersensitivity reaction to fungal infection. Appear as raised, boggy/spongy lesions, often tender and covered with exudate. Can be associated with posterior cervical lymphadenopathy.
4. **Diagnosis:** Can be made clinically, since oral antifungal therapy is indicated, but tinea capitis should be confirmed by examining KOH preparation under direct microscopic examination or culture of broken-off and surrounding hair.
5. **Treatment<sup>9</sup>:** First-line therapy includes oral griseofulvin for 10–12 weeks (which should be taken with fatty foods for improved absorption) and terbinafine, which is administered for 6 weeks. Topical antifungals will not be curative. All family members, particularly other children, should be examined carefully for subtle infection and treated. Selenium sulfide 2.5% shampoo may shorten the period of shedding of fungal organisms and reduce infection of unaffected family members.  
Kerion: Same treatment as above. Patients with intractable pruritus or intense edema should be treated with oral steroids for 2–3 weeks to reduce risk of further scarring or permanent hair loss. Bacterial cultures should be sent in children with fever and signs of cellulitis, and treatment should be initiated with systemic antistaphylococcal antibiotics.

## B. Alopecia Areata (Fig. 8-32, color)

1. **Clinical presentation:** Chronic inflammatory (probably autoimmune) disease that starts with small bald patches and normal-appearing underlying skin. New lesions may demonstrate subtle erythema and be pruritic. Bald patches may enlarge to involve large areas of the scalp or other hair-bearing areas. Many experience good hair regrowth within 1–2 years, although most will relapse. A minority progress to total loss of all scalp (alopecia totalis) and/or body hair (alopecia universalis).
2. **Diagnosis:** Usually clinical diagnosis. Biopsy is necessary in rare cases.

3. **Treatment<sup>10</sup>:** First-line therapy is topical and occasionally intralesional steroids. Minoxidil, anthralin, contact sensitization, and ultraviolet light therapy are second line. No evidence-based data that any therapy is better than placebo, so treatments with significant risk of toxicity should be avoided, particularly in children. Older children, adolescents, and young adults with long-standing localized areas of hair loss have the best prognosis.

#### C. Telogen Effluvium (Fig. 8-33, color)

1. **Pathogenesis:** Most common cause of diffuse hair loss, usually after stressful state (major illnesses or surgery, pregnancy, severe weight loss). Mature hair follicles switch prematurely to the telogen (resting) state, with shedding within 3 months.
2. **Clinical presentation:** Diffuse hair thinning 3 months after stressful event. May not be clinically obvious to an outsider until more than 20% of hair is lost.
3. **Treatment:** Self-limited, regrowth usually occurs over the next few months.

#### D. Traction Alopecia (Fig. 8-34, color)

1. **Pathogenesis:** Result of hairstyles that apply tension for long periods of time.
2. **Clinical presentation:** Noninflammatory linear areas of hair loss at margins of hairline, part line, or scattered regions, depending on hairstyling procedures used.
3. **Treatment:** Avoidance of styling products or styles that result in traction. If traction remains for long periods, condition may progress to permanent scarring hair loss.

#### E. Trichotillomania

1. **Pathogenesis:** Alopecia due to compulsive urge to pull out one's own hair, resulting in irregular areas of incomplete hair loss. Alopecia notable mainly on the scalp; can involve eyebrows and eyelashes. Onset is usually after age 10 and should be distinguished from hair pulling in younger children that resolves without treatment in most cases.
2. **Clinical presentation:** Characterized by hair of differing lengths; area of hair loss can be unusual in shape.
3. **Treatment:** Many cases require behavioral modification. Adolescents may benefit from psychiatric evaluation; condition can be associated with anxiety, depression, and obsessive-compulsive disorder.

### VI. ACNE VULGARIS

#### A. Pathogenesis:

1. **Blockade of follicular opening from hyperkeratinization**
2. **Increased sebum production**
3. **Proliferation of *Propionibacterium acnes***
4. **Inflammation**
5. **Risk factors:** Androgens, family history, and stress. No strong evidence that dietary habits affect acne.

**B. Clinical presentation:****1. Noninflammatory lesions**

- a. Closed comedo (whitehead): Accumulation of sebum and keratinous material, resulting in white/skin-colored papules without surrounding erythema.
  - b. Open comedo (blackhead): Dilated follicles packed with keratinocytes, oils, and melanin.
- 2. Inflammatory lesions:** Papules, pustules, nodules, cysts. Typically appear later in the course of acne and vary from 1- to 2-mm micropapules to nodules >5 mm. Nodulocystic presentations are more likely to lead to permanent scarring and/or hyperpigmentation.

**C. Classification: Used to estimate severity, but not always practical in a clinical setting**

1. **Mild:** <20 comedones, <15 inflammatory lesions, or total <30
2. **Moderate:** 20–100 comedones, 15–50 inflammatory lesions, or total 30–125
3. **Severe:** >100 comedones, >50 inflammatory lesions, >5 cysts, or total >125
4. **Clinician should also consider** the number of skin areas involved and extent in each area (e.g., face, back, chest, and occasionally arms, legs, scalp)

**D. Treatment<sup>11,12</sup> (Table 8-2 and Table 8-3)**

1. **Skin care:** Gentle nonabrasive cleaning. Avoid picking or popping lesions. Vigorous scrubbing and abrasive cleaners can worsen acne.
2. **Topical retinoids:** First-line therapy for mild to moderate acne. Normalize follicular keratinization and decrease inflammation. A small amount should be applied as a thin layer to all affected areas. Can cause irritation and dryness of skin. Retinoids should probably be used at a different time of day than benzoyl peroxide to minimize risk of irritation, especially when therapy is initiated.
3. **Topical antimicrobials:**
  - a. Erythromycin, clindamycin, dapsone. Avoid topical antibiotics as monotherapy, and probably should not be used when an oral antibiotic is already being used.
  - b. Benzoyl peroxide (BPO): Oxidizing agent with antibacterial and mild comedolytic properties. Decreases antibiotic resistance when used with oral antibiotics. Can bleach hair, clothing, towels. Washes may be most convenient formulation, because they can be rinsed off in the shower.
  - c. Azelaic acid.
4. **Oral antibiotics:** First line for moderate to severe inflammatory acne. Avoid oral antibiotics as monotherapy, owing to increased antibiotic resistance. Doxycycline and minocycline are first line (although it is difficult to obtain 100-mg formulations of doxycycline). Use with BPO and/or topical retinoids. Try to limit length of therapy, and reassess clinically at 6–12 weeks.
5. **Oral contraceptives:** Good alternative for females who have sudden onset of moderate to severe acne and have not responded to conventional first-line therapy. Should not be used as monotherapy. Reduces sebum production and androgen levels.

TABLE 8-2

## TOPICAL AND SYSTEMIC ANTIBIOTICS USED TO TREAT ACNE

Antibiotic	Characteristics
<b>TOPICAL</b>	
Erythromycin	<i>Propionibacterium acnes</i> very sensitive; least lipophilic
Clindamycin	<i>P. acnes</i> very sensitive; more lipophilic than erythromycin but less than benzoyl peroxide (BPO)
BPO +erythromycin	<i>P. acnes</i> very sensitive; most lipophilic topical agent; less irritating than BPO alone
BPO +clindamycin	Similar to characteristics for BPO + erythromycin
Azelaic acid	<i>P. acnes</i> sensitive; minimal lipophilia; can reduce abnormal desquamation
Metronidazole	<i>P. acnes</i> not sensitive; has antiinflammatory properties
BPO +glycolic acid	Glycolic acid may enhance penetration and reduce abnormal desquamation
<b>SYSTEMIC</b>	
Doxycycline	Lipophilic; <i>P. acnes</i> very sensitive; can cause photosensitivity, gastrointestinal (GI) upset, esophagitis, pseudotumor cerebri; must be taken with food
Minocycline	Lipophilic; <i>P. acnes</i> very sensitive; more expensive; less photosensitivity and GI upset, can cause drug hypersensitivity syndrome, lupus-like syndrome, rare staining of skin and teeth
Tetracycline	<i>P. acnes</i> sensitive; inexpensive; can cause photosensitivity, GI upset, pseudotumor cerebri, tooth discoloration, and inhibited skeletal growth. Limit use in pregnant women and children <8 years. Must be taken on empty stomach.
Erythromycin	<i>P. acnes</i> resistance emerging; inexpensive; can cause GI upset; safe for young children and pregnant women
Trimethoprim-sulfamethoxazole	Lipophilic; <i>P. acnes</i> very sensitive; severe erythema multiforme and toxic epidermal necrolysis limit use; potential alternative for patients allergic to other antibiotics
Clindamycin	Somewhat lipophilic; <i>P. acnes</i> very sensitive; pseudomembranous colitis limits use

From Leyden JJ. Therapy for acne vulgaris. *N Engl J Med*. 1997;16:1156-1162.

6. **Oral isotretinoin (Accutane):** Reserved for patients with severe nodular, cystic, or scarring acne who do not respond to traditional therapy. Should be managed by a dermatologist. Significantly decreases sebum production, inflammation, *P. acnes*, and can diminish scarring. Most patients have complete resolution of their acne after 16–20 weeks of use.

a. Side effects:

- (1) Teratogenicity: Patients and physicians are mandated by the FDA to comply with iPledge, a computerized risk management program designed to eliminate fetal exposure to isotretinoin. Female patients of child-bearing potential must use two forms of birth control and routinely get pregnancy tests.
- (2) Hepatotoxicity, hyperlipidemia, and bone marrow suppression. A complete blood cell count (CBC), fasting lipid profile, and liver function tests should be obtained before initiation of therapy and repeated at 4 and 8 weeks.
- (3) Other: Myalgias, visual changes, pseudotumor cerebri.



TABLE 8-3

## ACNE TREATMENT ALGORITHM

	Acne Severity				
	Mild		Moderate		Severe
	Comedonal	Papular/Pustular	Papular/Pustular	Nodular	Nodular/Conglobate
First-line treatment	Topical retinoid	Topical retinoid + Topical antibiotic	Oral antibiotic + Topical retinoid +/- BPO	Oral antibiotic + Topical retinoid +/- BPO	Oral isotretinoin
Alternative treatments	Alternative topical retinoid <i>OR</i> Azelaic acid	Alternative topical antimicrobial agent <i>OR</i> + Alternative topical retinoid <i>OR</i> Azelaic acid	Alternative oral antibiotic + Alternative topical retinoid +/- BPO	Oral isotretinoin <i>OR</i> Alternative oral antibiotic + Alternative topical retinoid +/- BPO	High-dose oral antibiotic + Topical retinoid + BPO
Alternative treatments for females			Oral anti-androgen + Topical retinoid +/- Topical antimicrobial	Oral antiandrogen + Topical retinoid +/- Oral antibiotic +/- Topical antimicrobial	High-dose oral antiandrogen + Topical retinoid +/- Topical antimicrobial
Maintenance treatment	Topical retinoid		Topical retinoid +/- BPO		

BPO, Benzoyl peroxide.

Modified from Gollnick H, Cunliffe W, Berson D, et al. Management of acne: a report from a Global Alliance to Improve Outcomes in Acne. *J Am Acad Dermatol*. 2003;49(suppl 1):S1-S37.

**VII. COMMON NEONATAL DERMATOLOGIC CONDITIONS (FIGS. 8-35 TO 8-44)****A. Erythema Toxicum Neonatorum (ETN) (Fig. 8-36, color)**

Most common rash of full-term infants; incidence declines with lower birth weight and prematurity. Appears as small erythematous macules and papules that evolve into pustules on erythematous bases. Rash occurs most often by 24–48 hours of life but can be present at birth or emerge as late as 2–3 weeks. Self-limited, resolves within 5–7 days; recurrences possible. Pustular fluid reveals eosinophils.

**B. Transient Neonatal Pustular Melanosis (Figs. 8-37 and 8-38, color)**

More commonly affects full-term infants with darker pigmentation. At birth, appears as small pustules on nonerythematous bases that rupture and leave erythematous/hyperpigmented macules with a collarette of scale. Self-limited; macules fade over weeks to months. Pustular fluid reveals neutrophils.

**C. Miliaria (Heat Rash, Prickly Heat) (Fig. 8-39, color)**

Common newborn rash associated with warmer climates, incubator use, or occlusion with clothes/dressings. Appears as small erythematous papules or pustules usually on face, scalp, or intertriginous areas. Due to obstruction of eccrine sweat ducts in the stratum corneum. Rash resolves when infant is placed in cooler environment or tight clothing/dressings are removed.

**D. Milia (Fig. 8-40, color)**

Common newborn rash. Appears as 1- to 3-mm white/yellow papules, frequently found on nose and face; due to retention of keratin and sebaceous materials in pilosebaceous follicles. Self-limited, resolves within first few weeks of life.

**E. Neonatal Acne (Fig. 8-41, color)**

Seen in 20% of infants. Appears as inflammatory papules or pustules without comedones, usually on face and scalp. Secondary to effect of maternal and endogenous androgens on infant's sebaceous glands. Peaks around 1 month, resolves within a few months, usually without intervention. Does not increase risk of acne as an adolescent.

**F. Seborrheic Dermatitis (Cradle Cap) (Figs. 8-42 and 8-43, color)**

Common rash characterized by erythematous plaques with greasy yellow scales. Located in areas rich with sebaceous glands, such as scalp, cheeks, ears, eyebrows, intertriginous areas, diaper area. Unknown etiology. Can be seen in newborns, more commonly in infants 1–4 months old. Self-limited and resolves within a few weeks to months. Can remove scales on scalp with soft brush/fine comb. In more severe cases, antifungal shampoos or low-potency topical steroid can shorten the course.

**G. Mongolian Spots**

Most common pigmented lesion of newborns, usually seen in babies with darker skin tone. Appear as blue/gray macules without definite

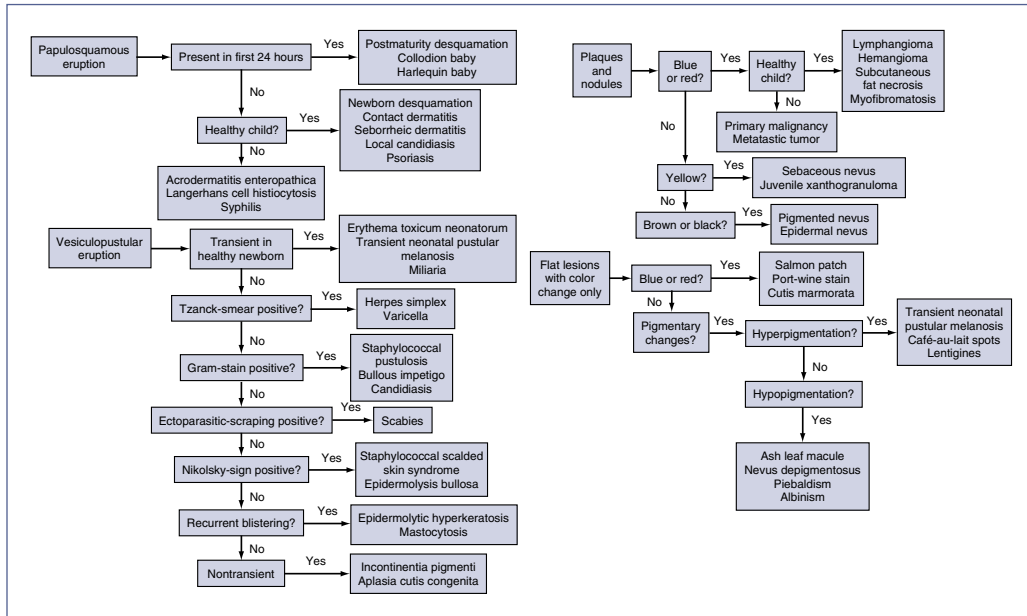


FIGURE 8-35

Evaluation of neonatal rashes. (Modified from Cohen BA. Atlas of Pediatric Dermatology. 3rd ed. St Louis: Mosby, 2005:62.)

borders, frequently seen on sacral regions or shoulders. Due to delayed disappearance of dermal melanocytes. Spots typically fade within first few years of life, with majority resolved by age 10 years. Can be mistaken for child abuse. Should be differentiated from other pigmented lesions (e.g., blue nevi, nevus of Ota, nevus of Ito).

#### **H. Diaper Candidiasis (Fig. 8-44, color)**

Very common diaper rash, characterized by a red, raised rash with small raised and infected areas around the periphery called *satellite lesions*. Etiology is usually irritation or seborrheic dermatitis that can become secondarily infected with *Candida*. Commonly seen in infancy during periods of diaper wearing. Can be minimized by keeping diaper area clean, as dry as possible, with frequent diaper changes and topical agents such as powders. Treatment with topical nystatin, miconazole, or clotrimazole is sufficient.

### **VIII. BULLOUS LESIONS: DIAGNOSIS AND TREATMENT (FIGS. 8-45 TO 8-47)**

#### **A. Impetigo**

1. **Pathogenesis:** Contagious bacterial infection of the skin, most commonly caused by *Staphylococcus aureus*, with a minority of cases caused by group A beta-hemolytic *Streptococcus*. Methicillin-resistant *S. aureus* (MRSA) impetigo in the community and in hospital settings is on the rise.
2. **Clinical presentation:**
  - a. Non-bullous impetigo: Papules that evolve into erythematous pustules or vesicles that break and form thick, honey-colored crusts and plaques. Commonly overlying insect bites, abrasions, or other site of trauma. Usually found on face and extremities. Can have regional lymphadenopathy, but rare to have systemic symptoms.
  - b. Bullous impetigo: Painless vesicles that evolve into flaccid bullae with clear/yellow fluid that turns darker; leave yellow/brown crust when bullae rupture. Seen more in infants and young children. Caused by exfoliative toxin A from *S. aureus*.
3. **Epidemiology:** Most common in children 2–5 years of age, but seen in older children and adults. Risk factors include crowding, contact sports, and poor hygiene.
4. **Treatment:**
  - a. Practice good hand hygiene. Many children may be colonized with organism before infection develops, so treat minor injuries and insect bites early to minimize infection risk. Evaluate other family members for infection. Consider bleach baths, BPO wash, other antiseptics, cleaning athletic equipment, and other prophylactic measures in patients with recurrent infections.
  - b. Non-bullous impetigo: Topical antibiotics (mupirocin) if lesions are limited
  - c. Bullous impetigo or widespread non-bullous impetigo: Oral antibiotics with gram-positive coverage; consider MRSA coverage (dicloxacillin, cephalexin, clindamycin).

## B. Autoimmune Bullous Diseases

1. **Very rare in children** but should be considered if bullous lesions do not respond to standard therapy. Suspicion for any of the following should warrant referral to a dermatologist for diagnosis and management.
2. **Pemphigus vulgaris (Fig. 8-45, color):**
  - a. Pathogenesis: IgG autoantibodies to adhesion molecules desmoglein-1 and desmoglein-3, which interrupts integrity of epidermis and/or mucosa and results in extensive blister formation.
  - b. Clinical presentation: Flaccid bullae that start in the mouth and spread to face, scalp, trunk, extremities, and other mucosal membranes. Positive Nikolsky sign. Ruptured blisters are painful and prone to secondary infection. Can lead to impaired oral intake if there is significant oral mucosal involvement.
  - c. Treatment: Immunosuppressants (systemic glucocorticoids, rituximab, intravenous immunoglobulin [IVIG])
3. **Pemphigus foliaceus:**
  - a. Pathogenesis: IgG autoantibodies to desmoglein-1. Antibodies bind to the same antigen as in bullous impetigo and staphylococcal scalded skin syndrome, so lesions are superficial and rupture easily. Can be triggered by certain drugs, including thiol compounds and penicillins.
  - b. Clinical presentation: Scaling, crusting erosions on erythematous base that appear on face, scalp, trunk, and back. No mucosal involvement. Lesions are more superficial than in pemphigus vulgaris.
  - c. Treatment: Immunosuppressants
4. **Bullous pemphigoid:**
  - a. Pathogenesis: Autoantibodies to the epithelial basement membrane that results in an inflammatory cascade and causes separation of epidermis from dermis and epithelium from subepithelium.
  - b. Clinical presentation: Prodrome of inflammatory lesions that progresses into large (1–3 cm), tense, extremely pruritic bullae on trunk, flexural regions, and intertriginous areas. A minority have oral mucosal lesions. Negative Nikolsky sign.
  - c. Treatment: Immunosuppressants.
5. **Dermatitis herpetiformis:**
  - a. Pathogenesis: Strong genetic predisposition and link to gluten intolerance/celiac disease. IgA deposits found in dermal papillae.
  - b. Clinical presentation: Symmetric, intensely pruritic papulovesicles clustered on extensor surfaces.
  - c. Treatment: Dapsone, strict gluten-free diet.

## C. Burns (see Chapter 4)

## D. Contact Dermatitis

1. **Irritant dermatitis:** Exposure to physical, chemical, or mechanical irritants to the skin. Top two causes in children are dry skin dermatitis and diaper dermatitis.

**2. Allergic dermatitis (Fig. 8-46, color):**

- a. Pathogenesis: T-cell-mediated immune reaction in response to an environmental trigger that comes into contact with the skin. After initial exposure causes sensitization, an allergic response occurs with subsequent exposures.
- b. Allergens: Common antigens are *Toxicodendron* spp. (poison ivy, poison oak, poison sumac). Also nickel, cobalt, gold, dyes, formaldehyde.
- c. Clinical presentation: Pruritic erythematous dermatitis that can progress to a chronic stage involving scaling, lichenification, and pigmentary changes. Initial reaction occurs after a sensitization period of 7–10 days in susceptible individuals. Antigen reexposure causes a more rapid reactivation reaction.
  - (1) Poison ivy (Fig. 8-47, color): Exposure to urushiol, the allergenic substance in poison ivy, causes streaks of erythematous papules, pustules, and vesicles. Highly pruritic, can become edematous, especially if rash is on face or genitals. In extreme cases, anaphylaxis can occur.

3. **Diagnosis:** Careful history taking. Patch testing may also be helpful.

**4. Treatment:**

- a. Remove causative agent. For poison ivy contact, remove clothing and wash skin with mild soap and water as soon as possible.
- b. Mild dermatitis: Topical steroids.
- c. Widespread or severe dermatitis: Systemic steroids for 2–3 weeks. There is no role for short courses of steroids (e.g., Medrol dose pack), because eruption will flare when drug is stopped.


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# Chapter 9

## Development, Behavior, and Mental Health

Melissa Kwan, MD

 See additional content on Expert Consult

### I. WEBSITES

ADHD: [www.chadd.org](http://www.chadd.org)

ADHD Medication Guide: [www.ADHDMedicationGuide.com](http://www.ADHDMedicationGuide.com)

American Academy of Pediatrics—Developmental and Behavioral Pediatrics: [www.dbpeds.org](http://www.dbpeds.org)

Disability Programs and Services: [www.disability.gov](http://www.disability.gov)

Learning Disabilities Association of America: [www.ldanatl.org](http://www.ldanatl.org)

Intellectual Disability: [www.theaclink.org](http://www.theaclink.org)

Bright Futures: [www.brightfutures.org](http://www.brightfutures.org)

National Early Childhood Technical Assistance Center: [www.nectac.org](http://www.nectac.org)

Reach Out and Read: [www.reachoutandread.org](http://www.reachoutandread.org)

Child and Adolescent Psychiatry Practice Parameters: [www.aacap.org](http://www.aacap.org)

Mental health patient and provider handouts: [www.nimh.nih.gov](http://www.nimh.nih.gov)

### II. INTRODUCTION

#### A. Development

1. **Development can be divided into five major streams:** Visual-motor, language, motor, social, and adaptive.
2. **Abnormal development** in one stream increases the risk for abnormality in another and should prompt a careful assessment of all streams.
3. **Developmental diagnosis** is a functional description and classification and does not specify an etiology or medical diagnosis.
4. **Developmental assessment** is based on the premise that milestone acquisition occurs at a specific rate in an orderly and sequential manner.
  - a. A good milestone is one that can easily be assessed by parents or a provider, and also one that occurs in a narrow time window.
  - b. When development is not progressing normally, the pattern of abnormal development may include delay, deviancy, and/or dissociation.

### III. DEFINITIONS

#### A. Developmental Quotient (DQ)

1. **A calculation that reflects the rate of development** in any given stream and represents the percentage of normal development present at the time of testing.
$$DQ = (\text{Developmental Age} / \text{Chronologic Age}) \times 100$$
2. **Two separate developmental assessments** over time are more predictive than a single assessment.

**B. Delay**

1. **Performance significantly below average (DQ < 70) in a given area of skill.** May occur in a single stream or several streams.

**C. Deviancy**

1. **Atypical development within a single stream**, such as developmental milestones occurring out of sequence. Deviancy does not necessarily imply abnormality but should alert one to the possibility that problems may exist. Example: An infant who rolls at an early age may have abnormally increased tone.
2. **Deviancy may also denote emergence of a presentation that is not typically part of the developmental sequence.** Example: A toddler showing no interest in peers.

**D. Dissociation**

1. **A substantial difference in the rate of development between two or more streams.** Example: Motor delay relative to cognition seen in some children with cerebral palsy.

**E. Gross Motor Skills**

1. **Descriptions of posture and locomotion**—in general, how a child moves from one location to another.

**F. Fine-Motor and Visual-Motor Problem-Solving Skills**

1. **Upper extremity and hand manipulative abilities and hand-eye coordination.** These skills depend to some degree on an intact motor substrate and require a given level of nonverbal cognitive ability.

**G. Language**

1. **The ability to understand and communicate with another person.**
2. **In the absence of a communication disorder or significant hearing impairment**, language development represents the best predictor of intellectual performance.

**H. Social Skills**

1. **Communicative in origin and represent the cumulative impact of language comprehension and problem-solving skills.** Social behaviors might be considered the functional expression resulting from the interaction of these two streams of development.

**I. Adaptive Skills**

1. **Skills concerned with self-help or activities of daily living.**

**IV. GUIDELINES FOR NORMAL DEVELOPMENT AND BEHAVIOR****A. Developmental Milestones (Table 9-1)****B. Reach Out and Read Milestones of Early Literacy (Table 9-2)****C. Age-Appropriate Behavioral Issues in Infancy and Early Childhood (Table 9-3)**



TABLE 9-1

## DEVELOPMENTAL MILESTONES

Age	Gross Motor	Visual-Motor/ Problem-Solving	Language	Social/Adaptive
1 mo	Raises head from prone position	Visually fixes, follows to midline, has tight grasp	Alerts to sound	Regards face
2 mo	Holds head in midline, lifts chest off table	No longer clenches fists tightly, follows object past midline	Smiles socially (after being stroked or talked to)	Recognizes parent
3 mo	Supports on forearms in prone position, holds head up steadily	Holds hands open at rest, follows in circular fashion, responds to visual threat	Coos (produces long vowel sounds in musical fashion)	Reaches for familiar people or objects, anticipates feeding
4 mo	Rolls over, supports on wrists, shifts weight	Reaches with arms in unison, brings hands to midline	Laughs, orients to voice	Enjoys looking around
6 mo	Sits unsupported, puts feet in mouth in supine position	Unilateral reach, uses raking grasp, transfers objects	Babbles, ah-goo, razz, lateral orientation to bell	Recognizes that someone is a stranger
9 mo	Pivots when sitting, crawls well, pulls to stand, cruises	Uses immature pincer grasp, probes with forefinger, holds bottle, throws objects	Says “mama, dada” indiscriminately, gestures, waves bye-bye, understands “no”	Starts exploring environment, plays gesture games (e.g., pat-a-cake)
12 mo	Walks alone	Uses mature pincer grasp, can make a crayon mark, releases voluntarily	Uses two words other than “mama, dada” or proper nouns, jargoning (runs several unintelligible words together with tone or inflection), one-step command with gesture	Imitates actions, comes when called, cooperates with dressing
15 mo	Creeps up stairs, walks backward independently	Scribbles in imitation, builds tower of 2 blocks in imitation	Uses 4–6 words, follows one-step command without gesture	15–18 mo: uses spoon and cup
18 mo	Runs, throws objects from standing without falling	Scribbles spontaneously, builds tower of 3 blocks, turns two or three pages at a time	Mature jargoning (includes intelligible words), 7–10 word vocabulary, knows 5 body parts	Copies parent in tasks (sweeping, dusting), plays in company of other children
24 mo	Walks up and down steps without help	Imitates stroke with pencil, builds tower of 7 blocks, turns pages one at a time, removes shoes, pants, etc.	Uses pronouns (I, you, me) inappropriately, follows two-step commands, 50-word vocabulary, uses 2-word sentences	Parallel play

Continued

TABLE 9-1

## DEVELOPMENTAL MILESTONES (Continued)

Age	Gross Motor	Visual-Motor/ Problem-Solving	Language	Social/Adaptive
3 yr	Can alternate feet going up steps, pedals tricycle	Copies a circle, undresses completely, dresses partially, dries hands if reminded, unbuttons	Uses minimum of 250 words, 3-word sentences, uses plurals, knows all pronouns, repeats two digits	Group play, shares toys, takes turns, plays well with others, knows full name, age, gender
4 yr	Hops, skips, alternates feet going down steps	Copies a square, buttons clothing, dresses self completely, catches ball	Knows colors, says song or poem from memory, asks questions	Tells "tall tales," plays cooperatively with a group of children
5 yr	Skips alternating feet, jumps over low obstacles	Copies triangle, ties shoes, spreads with knife	Prints first name, asks what a word means	Plays competitive games, abides by rules, likes to help in household tasks

From Capute AJ, Biehl RF. Functional developmental evaluation: prerequisite to habilitation. *Pediatr Clin North Am.* 1973;20:3; Capute AJ, Accardo PJ. Linguistic and auditory milestones during the first two years of life: a language inventory for the practitioner. *Clin Pediatr.* 1978;17:847; and Capute AJ, Shapiro BK, Wachtel RC, et al. The Clinical Linguistic and Auditory Milestone Scale (CLAMS): identification of cognitive defects in motor delayed children. *Am J Dis Child.* 1986;140:694. Rounded norms from Capute AJ, Palmer FB, Shapiro BK, et al. Clinical Linguistic and Auditory Milestone Scale: prediction of cognition in infancy. *Dev Med Child Neurol.* 1986;28:762.

TABLE 9-2

## REACH OUT AND READ MILESTONES OF EARLY LITERACY

Age	Motor	Cognitive
6–12 mo	Reaches for books, turns pages with help	Looks at pictures, pats pictures
12–18 mo	Carries book, holds book with help, turns several board pages at a time	Points to pictures with a single finger, points to specific items on page, gives book to adult
18–24 mo	Turns one board page at a time	Repeats and retells parts of known stories
24–36 mo	Begins to turn paper pages	Looks at favorite books on own, repeats and retells whole phrases and stories, associates pictures with text of story
3 yr	Turns paper pages easily	Growing attention span, recites favorite stories, begins to identify single letters
4 yr and older	Writes name	Uses past tense and plurals, answers "what will happen next"

From Reach Out and Read National Center: [www.reachoutandread.org](http://www.reachoutandread.org).

TABLE 9-3

AGE-APPROPRIATE BEHAVIORAL ISSUES IN INFANCY AND EARLY CHILDHOOD

Age	Behavioral Issue	Symptoms	Guidance
1–3 mo	Colic	Paroxysms of fussiness/ crying, 3+ hr per day, 3+ days per wk, may pull knees up to chest, pass flatus	Crying usually peaks at 6 wk and resolves by 3–4 mo. Prevent overstimulation; swaddle infant; use white noise, swing, or car rides to soothe. Avoid medication and formula changes. Encourage breaks for the primary caregiver.
3–4 mo	Trained night feeding	Night awakening	Comfort quietly, avoid reinforcing behavior (i.e., avoid night feeds). Do not play at night. Introducing cereal or solid food does not reduce awakening. Develop a consistent bedtime routine. Place baby in bed while drowsy and not fully asleep.
9 mo	Stranger anxiety/separation anxiety	Distress when separated from parent or approached by a stranger	Use a transitional object (e.g., special toy, blanket); use routine or ritual to separate from parent; may continue until 24 mo but can reduce in intensity.
	Developmental night waking	Separation anxiety at night	Keep lights off. Avoid picking child up or feeding. May reassure verbally at regular intervals or place a transitional object in crib.
12 mo	Aggression	Biting, hitting, kicking in frustration	Say “no” with negative facial cues. Begin time out (1 minute per year of age). No eye contact or interaction, place in a nonstimulating location. May restrain child gently until cooperation is achieved.
	Need for limit setting	Exploration of environment, danger of injury	Avoid punishing exploration or poor judgment. Emphasize child-proofing and distraction.
18 mo	Temper tantrums	Occur with frustration, attention-seeking rage, negativity/refusal	Try to determine cause, react appropriately (i.e., help child who is frustrated, ignore attention-seeking behavior). Make sure child is in a safe location.
24 mo	Toilet training	Child needs to demonstrate readiness: shows interest, neurologic maturity (i.e., recognizes urge to urinate or defecate), ability to walk to bathroom and undress self, desire to please/ imitate parents, increasing periods of daytime dryness.	Age range for toilet training is usually 2–4 yr. Give guidance early; may introduce potty seat but avoid pressure or punishment for accidents. Wait until the child is ready. Expect some periods of regression, especially with stressors.

Continued

TABLE 9-3

AGE-APPROPRIATE BEHAVIORAL ISSUES IN INFANCY AND EARLY CHILDHOOD (Continued)

Age	Behavioral Issue	Symptoms	Guidance
24–36 mo	New sibling	Regression, aggressive behavior	Allow for special time with parent, 10–20 min daily of one-on-one time exclusively devoted to the older sibling(s). Child chooses activity with parent. No interruptions. May not be taken away as punishment.
36 mo	Nightmares	Awakens crying, may or may not complain of bad dream	Reassure child, explain that he or she had a bad dream. Leave bedroom door open, use a nightlight, demonstrate there are no monsters under the bed. Discuss dream the following day. Avoid scary movies or television shows.
	Night terrors	Agitation, screaming 1–2 hr after going to bed. Child may have eyes open but not respond to parent. May occur at same time each night.	May be familial, not volitional. <i>Prevention:</i> For several nights, awaken child 15 min before terrors typically occur. Avoid overtiredness. <i>Acute:</i> Be calm; speak in soft, soothing, repetitive tones; help child return to sleep. Protect child against injury.

From Dixon SD, Stein MT. *Encounters with Children: Pediatric Behavior and Development*. St Louis: Mosby, 2000.

## V. DEVELOPMENTAL SCREENING AND EVALUATION

### A. Developmental Screening Guidelines

- Developmental surveillance should be included in every well-child visit, and any concerns should be addressed immediately.** Many parents do not differentiate between development and behavior, and many delays manifest through behavior.
  - Do you have any concerns about your child's development? Behavior? Learning?
  - What changes have you seen in your child's development since our last visit?
  - How old would you say your child acts?
- Developmental surveillance should occur at every well-child visit.** Standardized developmental screening should be administered at 9-month, 18-month, and 30-month well-child visits. If a 30-month visit is not possible, this screening can be done at the 24-month visit.
- Specific screening for autism should occur at the 18-month and 24-month visits.**<sup>2</sup>

### B. Commonly Used Developmental Screening and Assessment Tools

- Appropriate screening tests vary with age and suspected diagnosis.** Significant delays on screening merit referral for formal assessment. Several developmental screening and assessment tools are available (Table 9-4).

TABLE 9-4

## DEVELOPMENTAL AND MENTAL HEALTH SCREENING TESTS BY DIAGNOSIS

Diagnosis	Screening Tests	Age	Administration Time	Completed By	Weblink
Cognitive/motor development	Ages and Stages Questionnaire (ASQ)	4–60 mo	10–15 min	Parent	<a href="http://www.agesandstages.com">http://www.agesandstages.com</a>
	Parents Evaluation of Developmental Status (PEDS)	0–8 yr	2–10 min	Parent	<a href="http://www.pedstest.com">http://www.pedstest.com</a>
	Denver II Developmental Screening Test	0–6 yr	10–12 min	Clinician	
Autism spectrum disorders	Capute Scales (CAT/CLAMS)	3–36 mo	15–20 min	Clinician	
	Modified Checklist for Autism in Toddlers (M-CHAT)	16–48 mo	5–10 min	Parent	<a href="http://www.firstsigns.org/downloads/m-chat.PDF">http://www.firstsigns.org/downloads/m-chat.PDF</a>
	Childhood Autism Rating Scale (CARS)	>2 yr	20–30 min	Clinician	
Attention deficit/hyperactivity disorder (ADHD)	Vanderbilt Scales	6–12 yr	10–15 min	Parent and teachers	<a href="http://www.brightfutures.org/mentalhealth/pdf/professionals/bridges/adhd.pdf">http://www.brightfutures.org/mentalhealth/pdf/professionals/bridges/adhd.pdf</a>
Mental health	Connors Scales				<a href="http://psc.partners.org/psc_english.pdf">http://psc.partners.org/psc_english.pdf</a>
Depression	Pediatric Symptom Checklist (PSC)	4–18 yr	5–10 min	Parent or child/adolescent	<a href="http://psc.partners.org/psc_english.pdf">http://psc.partners.org/psc_english.pdf</a>
	Center for Epidemiological Studies Depression Scale for Children (CES-DC)		5–10 min	Child/adolescent	<a href="http://www.brightfutures.org/mentalhealth/pdf/professionals/bridges/ces_dc.pdf">http://www.brightfutures.org/mentalhealth/pdf/professionals/bridges/ces_dc.pdf</a>

CAT, Clinical Adaptive Test; CLAMS, Clinical Linguistic and Auditory Milestone Scale.

Partially modified from American Academy of Pediatrics. Identifying infants and young children with developmental disorders in the medical home: an algorithm for developmental surveillance and screening. *Pediatrics*. 2006;118:405-420.

2. **Capute Scales:** Assessment tools that give quantitative DQs for visual-motor/ problem-solving, and language abilities. The CLAMS (Clinical Linguistic and Auditory Milestone Scale) was developed for assessing language milestones from birth to age 36 months. The CAT (Clinical Adaptive Test) consists of problem-solving items for ages birth–36 months, adapted from standardized infant psychological tests.
3. **Denver II Developmental Assessment:** Tool for screening the apparently normal child from 0–6 years of age. Screens in four areas: personal-social, fine motor, gross motor, and language. For children born before 38 weeks' gestation, age should be corrected for prematurity up to age 2 years. A child fails a Denver screen if he or she has two or more delays noted. Indications for referral are a failed test or a classification of untestable on two consecutive screenings.
4. **Ages and Stages Questionnaire (ASQ):** Parent-based questionnaire for children aged 4–60 months. Benefits of parent-based questionnaires include increased time efficiency (parents can fill these out while waiting) and providing an opportunity to document milestones that are difficult to assess in the office or that children are less likely to perform in an unfamiliar setting.
5. **Parents' Evaluation of Developmental Status (PEDS):** Parent-based questionnaire for children up to 8 years of age.
6. **Goodenough-Harris Draw-a-Person Test:** Give the child a pencil and a sheet of blank paper. Instruct the child to “draw a person; draw the best person you can.” Use scoring guidelines to assess drawing and compare with norms for age. [See Box EC 9-A on Expert Consult.](#)
7. **Gesell figures (Fig. 9-1):** Examiner *should not* demonstrate drawing figures for the child.
8. **Gesell block skills (Fig. 9-2):** Examiner *should* demonstrate block structures for the child. [Fig. 9-2](#) includes developmental age at which each structure can usually be accomplished.

## VI. MEDICAL EVALUATION OF DEVELOPMENTAL DISORDERS

### A. History

1. **Prenatal and birth:** Toxins, trauma, prematurity, infection
2. **Past medical problems:** Trauma, infection, medication
3. **Developmental history:** Timing of milestone achievement, delayed skills, and loss of skills in all streams
4. **Behavioral history:** Social skills, eye contact, affection, hyperactivity, impulsivity, inattention, distractibility, self-regulation, perseveration, worries/avoidance, stereotypies, peculiar habits
5. **Educational history:** Need for special services, retention, established educational plans
6. **Family history:** Developmental disabilities, late talkers or walkers, trouble with education, attention deficit/hyperactivity disorder (ADHD), seizures, tics

### B. Physical Examination

1. **General:** Height, weight, head circumference, cardiac murmurs, midline defects

## BOX EC 9-A

## GOODENOUGH-HARRIS DRAW-A-PERSON TEST SCORING

General:	<input type="checkbox"/> Head present
	<input type="checkbox"/> Legs present
	<input type="checkbox"/> Arms present
Trunk:	<input type="checkbox"/> Present
	<input type="checkbox"/> Length greater than breadth
	<input type="checkbox"/> Shoulders
Arms/legs:	<input type="checkbox"/> Attached to trunk
	<input type="checkbox"/> At correct point
Neck:	<input type="checkbox"/> Present
	<input type="checkbox"/> Outline of neck continuous with head, trunk, or both
Face:	<input type="checkbox"/> Eyes
	<input type="checkbox"/> Nose
	<input type="checkbox"/> Mouth
	<input type="checkbox"/> Nose and mouth in two dimensions
	<input type="checkbox"/> Nostrils
Hair:	<input type="checkbox"/> Present
	<input type="checkbox"/> On more than circumference; nontransparent
Clothing:	<input type="checkbox"/> Present
	<input type="checkbox"/> Two articles; nontransparent
	<input type="checkbox"/> Entire drawing (sleeves and trousers) nontransparent
	<input type="checkbox"/> Four articles
	<input type="checkbox"/> Costume complete
Fingers:	<input type="checkbox"/> Present
	<input type="checkbox"/> Correct number
	<input type="checkbox"/> Two dimensions; length, breadth
	<input type="checkbox"/> Thumb opposition
	<input type="checkbox"/> Hand distinct from fingers and arm
Joints:	<input type="checkbox"/> Elbow, shoulder, or both
	<input type="checkbox"/> Knee, hip, or both
Proportion:	<input type="checkbox"/> Head: 10%–50% of trunk area
	<input type="checkbox"/> Arms: Approximately same length as trunk
	<input type="checkbox"/> Legs: 1–2 times trunk length; width less than trunk width
	<input type="checkbox"/> Feet: To leg length
	<input type="checkbox"/> Arms and legs in two dimensions
	<input type="checkbox"/> Heel
Motor coordination:	<input type="checkbox"/> Lines firm and well connected
	<input type="checkbox"/> Firmly drawn with correct joining
	<input type="checkbox"/> Head outline
	<input type="checkbox"/> Trunk outline
	<input type="checkbox"/> Outline of arms and legs
	<input type="checkbox"/> Features
Ears:	<input type="checkbox"/> Present
	<input type="checkbox"/> Correct position and proportion

Continued

BOX EC 9-A

GOODENOUGH-HARRIS DRAW-A-PERSON TEST SCORING (Continued)

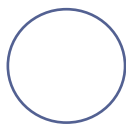
Eye detail:	<input type="checkbox"/> Brow or lashes
	<input type="checkbox"/> Pupil
	<input type="checkbox"/> Proportion
	<input type="checkbox"/> Glance directed front in profile drawing
Chin:	<input type="checkbox"/> Present; forehead
	<input type="checkbox"/> Projection
Profile:	<input type="checkbox"/> Not more than one error
	<input type="checkbox"/> Correct

Normal Values

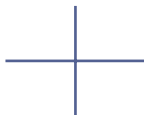
Age (Yr):	3	4	5	6	7	8	9	10	11	12	13
Score:	2	6	10	14	18	22	26	30	34	38	42



15 months	Imitates scribble
18 months	Scribbles spontaneously
2 years	Imitates stroke
2½ years	Differentiates horizontal and vertical stroke



3 yr



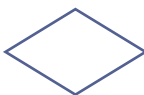
4 yr



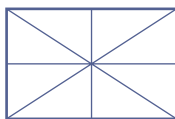
4½ yr



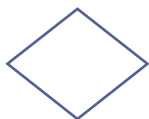
5 yr



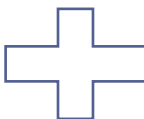
6 yr



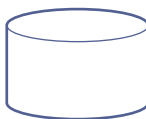
6 yr



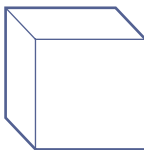
7 yr



8 yr



9 yr



11 yr

**FIGURE 9-1**

Gesell figures. (From Illingsworth RS. The Development of the Infant and Young Child, Normal and Abnormal. 5th ed. Baltimore: Williams & Wilkins, 1972:229-232; and Catell P. The Measurement of Intelligence of Infants and Young Children. New York: Psychological Corporation, 1960:97-261.)

## 2. Review for dysmorphic features.

3. **Age-directed neurologic examination:** Examination tailored to patient's age, including primitive reflexes for infants. See Tables EC 9-A and 9-B on Expert Consult.

## C. Laboratory Investigations, Imaging Studies, Other Tests

1. **Audiologic testing:** Indicated for all children with global developmental delay or any delay in communication or language.

TABLE EC 9-A

## PRIMITIVE REFLEXES

Primitive Reflexes	Elicitation	Response	Timing
Moro reflex (“embrace” response) of fingers, wrists, and elbows	<i>Supine</i> : sudden neck extension; allow head to fall back about 3 cm	Extension, adduction, and then abduction of UEs, with semiflexion	Present at birth; disappears by 3–6 mo
Galant reflex (GR)	<i>Prone suspension</i> : stroking paravertebral area from thoracic to sacral region	Produces truncal incurvature with concavity toward stimulated side	Present at birth; disappears by 2–6 mo
Asymmetric tonic neck reflex (ATNR, “fencer” response)	<i>Supine</i> : rotate head laterally about 45–90 degrees	Relative extension of limbs on chin side and flexion on occiput side	Present at birth; disappears by 4–9 mo
Symmetric tonic neck reflex (STNR, “cat” reflex)	<i>Sitting</i> : head extension/flexion	Extension of UEs and flexion of LEs/flexion of UEs and LE extension	Appears at 5 mo; not present in most normal children; disappears by 8–9 mo
Tonic labyrinthine supine (TLS)	<i>Supine</i> : neck extension (alters relation of labyrinths)	Tonic extension of trunk and LEs, shoulder retraction and adduction, usually with elbow flexion	Present at birth; disappears by 6–9 mo
Tonic labyrinthine prone (TLP)	<i>Prone</i> : neck flexion	Active flexion of trunk with protraction of shoulders	Present at birth; disappears by 6–9 mo
Positive support reflex (PSR)	Vertical suspension; bouncing hallual areas on firm surface	<i>Neonatal</i> : momentary LE extension followed by flexion <i>Mature</i> : extension of LEs and support of body weight	Present at birth; disappears by 2–4 mo Appears by 6 mo
Stepping reflex (SR, walking reflex)	Vertical suspension; hallual stimulation	Stepping gait	Disappears by 2–3 mo
Crossed extension reflex (CER)	Prone; hallual stimulation of LE in full extension	Initial flexion, adduction, then extension of contra-lateral limb	Present at birth; disappears by 9 mo
Plantar grasp	Stimulation of hallual areas	Plantar flexion grasp	Present at birth; disappears by 9 mo
Palmar grasp	Stimulation of palm	Palmar grasp	Present at birth; disappears by 9 mo
Lower extremity placing (LEP)	Vertical suspension; rubbing tibia or dorsum of foot against edge of tabletop	Initial flexion, then extension, then placing of LE on tabletop	Appears at 1 day
Upper extremity placing (UEP)	Rubbing lateral surface of forearm along edge of tabletop from elbow to wrist to dorsal hand	Flexion, extension, then placing of hand on tabletop	Appears at 3 mo
Downward thrust (DT)	Vertical suspension; thrust LEs downward	Full extension of LEs	Appears at 3 mo

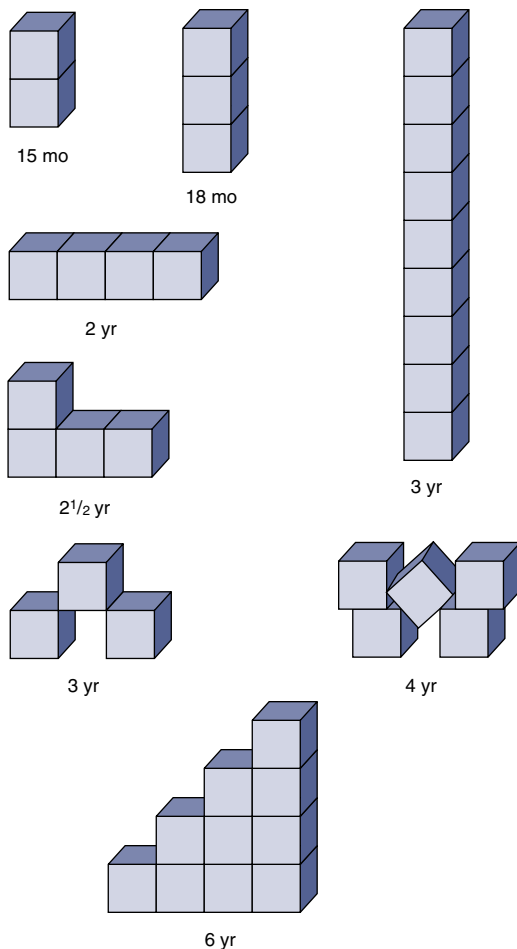
LE, Lower extremity; UE, upper extremity.

TABLE EC 9-B

## POSTURAL REACTIONS

Postural Reaction	Age of Appearance	Description	Importance
Head righting	6 wk–3 mo	Lifts chin from tabletop in prone position	Necessary for adequate head control and sitting
Landau response	2–3 mo	Extension of head, then trunk and legs when held prone	Early measure of developing trunk control
Derotational righting	4–5 mo	After passive or active head turning, body rotates to follow direction of head	Prerequisite to independent rolling
Anterior propping	4–5 mo	Arm extension anteriorly in supported sitting	Necessary for tripod sitting
Parachute	5–6 mo	Arm extension when falling	Facial protection when falling
Lateral propping	6–7 mo	Arm extension laterally in protective response	Allows independent sitting
Posterior propping	8–10 mo	Arm extension posteriorly	Allows pivoting in sitting

Modified from Milani-Comparetti A, Gidoni EA. Routine developmental examination in normal and retarded children. *Dev Med Child Neurol.* 1967;9:631; Capute AJ. Early neuromotor reflexes in infancy. *Pediatr Ann.* 1986;15:217; Capute AJ, Palmer FB, Shapiro BK, et al. Primitive reflex profile: a quantitation of primitive reflexes in infancy. *Dev Med Child Neurol.* 1984;26:375; and Palmer FB, Capute AJ. Developmental disabilities. In: Oski FA, ed. *Principles and Practice of Pediatrics.* Philadelphia: JB Lippincott, 1994.

**FIGURE 9-2**

Block skills. (From Capute AJ, Accardo PJ. The Pediatrician and the Developmentally Disabled Child: A Clinical Textbook on Mental Retardation. Baltimore: University Park Press, 1979:122.)

2. **Neuroimaging:** Consider if child has an abnormal neurologic examination or there is concern about head circumference growth velocity.
3. **Electroencephalogram:** If there is a history of seizure or concern about epilepsy syndrome
4. **Genetic studies may be considered based on individual history, family history, or physical examination:**
  - a. Microarray is the genetic test with the highest diagnostic yield and is considered the first-line cytogenetic test, although its cost should be carefully considered relative to its benefit to the family.
  - b. Karyotyping should be reserved for patients having signs of specific chromosomal syndromes (e.g., trisomy 13, 18, or 21).
  - c. Males with a history suggestive of X-linked inheritance may be considered for testing of one or more X-linked dominant (XLD) genes or screening of the entire X chromosome.
  - d. Females with severe impairment may be screened for MeCP2 mutations, regardless of whether the specific clinical features of Rett syndrome are present.
5. **Metabolic studies may be considered based on individual history, family history, or physical examination:**
  - a. Have a higher suspicion in children whose parents are consanguineous or have had children with similar problems or unexplained death or fetal demise.
  - b. These children may have multiple organ system dysfunction, failure to thrive, dietary selectivity, unusual odors, hearing loss, or episodic symptoms (seizures or encephalopathy).<sup>3</sup>

## VII. DISORDERS OF DEVELOPMENT

### A. Intellectual Disability

1. **Previously known as *mental retardation*, intellectual disability (ID) is characterized by three criteria:** deficits in intellectual functioning, deficits in adaptive functioning, and onset of these deficits during the developmental period. The adaptive deficit has to be in one or more domains of activities of daily living. (Note: Adaptive functioning determines level of support an individual needs, thereby defining the level of ID per DSM-5; [Table 9-5](#).)

### B. Communication Disorders

1. **Can be subdivided into language disorders, pragmatic communication disorders, and speech production disorders.**
2. **Differential diagnosis includes the previous disorders as well as intellectual disability, hearing loss, and autism or autism spectrum disorder.**

### C. Learning Disabilities (LDs)

1. **A heterogeneous group of disorders that manifest as significant difficulties in one or more of seven areas (as defined by the federal government):** basic reading skills, reading comprehension, oral expression, listening comprehension, written expression, mathematic calculation, and mathematic reasoning.

TABLE 9-5

SEVERITY LEVELS FOR INTELLECTUAL DISABILITY (INTELLECTUAL DEVELOPMENTAL DISORDER)

Severity Level	Conceptual Domain	Social Domain
Mild	For preschool children, there may be no obvious conceptual differences. For school-age children and adults, there are difficulties in learning academic skills involving reading, writing, arithmetic, time, or money, with support needed in one or more areas to meet age-related expectations. In adults, abstract thinking, executive function (i.e., planning, strategizing, priority setting, and cognitive flexibility), and short-term memory, as well as functional use of academic skills (e.g., reading, money management) are impaired. There is a somewhat concrete approach to problems and solutions compared with age-mates.	Compared with typically developing age-mates, the individual is immature in social interactions (e.g., difficulty in accurately perceiving peers' social cues). Communication, conversation, and language are more concrete or immature than expected for age. There may be difficulties regulating emotion and behavior in age-appropriate fashion; these difficulties are noticed by peers in social situations. There is limited understanding of risk in social situations; social judgment is immature for age, and the person is at risk of being manipulated by others (gullibility).
Moderate	All through development, the individual's conceptual skills lag markedly behind those of peers. For preschoolers, language and preacademic skills may develop slowly. For school-age children, progress in reading, writing, mathematics, and understanding of time and money occurs slowly across the school years and is markedly limited compared with that of peers. For adults, academic skill development is typically at an elementary level, and support is required for all use of academic skills in work and personal life. Ongoing assistance on a daily basis is needed to complete conceptual tasks of day-to-day life, and others may take over these responsibilities fully for the individual.	The individual shows marked differences from peers in social and communicative behavior across development. Spoken language is typically a primary tool for social communication but is much less complex than that of peers. Capacity for relationships is evident in ties to family and friends, and the individual may have successful friendships across life and sometimes romantic relations in adulthood. However, individuals may not perceive or interpret social cues accurately. Social judgment and decision-making abilities are limited, and caretakers must assist the person with life decisions. Friendships with typically developing peers are often affected by communication or social limitations. Significant social and communicative support is needed in work settings for success.
Severe	Attainment of conceptual skills is limited. The individual generally has little understanding of written language or of concepts involving numbers, quantity, time, and money. Caretakers provide extensive supports for problem solving throughout life.	Spoken language is quite limited in terms of vocabulary and grammar. Speech may be single words or phrases and may be supplemented through augmentative means. Speech and communication are focused on the here and now within everyday events. Language is used for social communication more than for explication. Individuals understand simple speech and gestural communication. Relationships with family members and familiar others are a source of pleasure and help.

TABLE 9-5

**SEVERITY LEVELS FOR INTELLECTUAL DISABILITY (INTELLECTUAL DEVELOPMENTAL DISORDER) (Continued)**

Severity Level	Conceptual Domain	Social Domain
Profound	Conceptual skills generally involve the physical world rather than symbolic processes. The individual may use objects in goal-directed fashion for self-care, work, and recreation. Certain visuospatial skills (e.g., matching and sorting based on physical characteristics) may be acquired. However, co-occurring motor and sensory impairments may prevent functional use of objects.	The individual has very limited understanding of symbolic communication in speech or gesture. He or she may understand some simple instructions or gestures. The individual expresses his or her own desires and emotions largely through nonverbal, nonsymbolic communication. The individual enjoys relationships with well-known family members, caretakers, and familiar others, and initiates and responds to social interactions through gestural and emotional cues. Co-occurring sensory and physical impairments may prevent many social activities.

Reprinted with permission from the American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Arlington, VA: APA, 2013.

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2. **Specific LDs are diagnosed when** the individual's achievement on standardized tests in a given area is substantially below that expected for age, schooling, and level of intelligence.<sup>4</sup>

#### D. Cerebral Palsy (CP)

1. **A disorder of movement and posture** resulting from a permanent nonprogressive lesion of the immature brain.
2. **Manifestations may change with brain growth and development.**
3. **The diagnosis of CP is made at a mean age of 13 months.**
4. **CP is classified in terms of physiologic and topographic characteristics as well as severity** (Table 9-6).<sup>5</sup> Classification is important because different classifications often have very different etiologies and associated deficits.

#### E. Autism Spectrum Disorders (ASDs)

See the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-5) for full diagnostic criteria.<sup>6</sup> For more detailed guidelines on evaluating for ASDs, see the American Academy of Pediatrics (AAP) practice guidelines.<sup>7</sup> Essential features are impaired social interaction and communication and a restricted group of activities and interests, with stereotyped behaviors, rituals, or mannerisms. Onset of abnormal functioning occurs in the early developmental period. A large proportion of autistic children function in the range of intellectual disability. Siblings of children with autism appear to be at greater risk, and males are disproportionately affected. Assessment scales like the Modified Checklist for

**TABLE 9-6**

**CLINICAL CLASSIFICATION OF CEREBRAL PALSY<sup>5</sup>**

Type	Pattern of Involvement
<b>I. SPASTIC (INCREASED TONE, CLASPED KNIFE, CLONUS, FURTHER CLASSIFIED BY DISTRIBUTION)</b>	
Hemiplegia	Ipsilateral arm and leg; arm worse than leg
Diplegia	Legs primarily affected
Quadriplegia	All four extremities impaired; legs worse than arms
Double hemiplegia	All four extremities; arms notably worse than legs
Monoplegia	One extremity, usually upper; probably reflects a mild hemiplegia
Triplegia	One upper extremity and both lower; probably represents a hemiplegia plus a diplegia or incomplete quadriplegia
<b>II. EXTRAPYRAMIDAL (LEAD PIPE OR CANDLE WAX RIGIDITY, VARIABLE TONE, <math>\pm</math> CLONUS)</b>	
Choreoathetosis, rigidity, dystonia	Complex movement/tone disorders reflecting basal ganglia pathology
Ataxia, tremor	Movement and tone disorders reflecting cerebellar origin
Hypotonia	Usually related to diffuse, often severe cerebral and/or cerebellar cortical damage

From Capute AJ, Accardo PJ, eds. *Cerebral Palsy: Developmental Disabilities in Infancy and Childhood*. 2nd ed. vol 2. Baltimore: Paul H. Brookes, 1996:83-86.

Autism in Toddlers (M-CHAT) and Childhood Autism Rating Scale (CARS) are available for screening (see [Table 9-4](#)).

**VIII. DISORDERS OF MENTAL HEALTH**

**A. Overview**

1. **Screening for mental health issues should occur at all routine well-child visits from early childhood through adolescence**, including history of mood symptoms and any behavioral issues.
2. **The Pediatric Symptom Checklist (PSC) is a general mental health checklist for ages 4–18 years that is filled out by a parent** and can be found in [Table 9-4](#). It screens for a broad array of mental health disorders, including conduct disorders, attention disorders, depression, anxiety, and adjustment disorders. See the DSM-5 for a more complete list of psychiatric diagnoses and full diagnostic criteria.<sup>6</sup>

**B. Attention Deficit/Hyperactivity Disorder (ADHD)**

**1. Epidemiology:**

- a. Affected 9.5% (5.4 million) of children in the United States in 2007.<sup>8</sup>
- b. Majority of children continue to meet diagnostic criteria through adolescence, and ADHD does not remit after onset of puberty. Symptoms may last through adulthood, with significant impairment noted.

**2. Assessment:**

- a. Diagnostic criteria: Inattention, impulsivity/hyperactivity that are more frequent and severe than typically observed in children of the same developmental age. Symptoms must persist for at least 6 months, occur



TABLE 9-7

## COMMONLY USED DRUGS

Antidepressants/Anxiolytics*	Antipsychotics*
Fluoxetine (Prozac)	Aripiprazole (Abilify)
Sertraline (Zoloft)	Haloperidol (Haldol)
Escitalopram (Lexapro)	Risperidone (Risperdal)
Mirtazapine (Remeron)	Quetiapine (Seroquel)

\*For more drug information, indications, and dosing please refer to the Formulary (Chapter 29).

before the age of 12 years, and be evident in two or more settings. See DSM-5 for updated diagnostic criteria.<sup>6,9</sup>

- b. Screen all children aged 4–18 who have academic and/or behavioral issues, and for comorbid conditions (oppositional defiant disorder [ODD], conduct disorder, depression, anxiety).<sup>10</sup>
  - c. Diagnosis is made using history, observation, and behavioral checklists such as the Vanderbilt Assessment Scale (see Table 9-4).
  - d. If the medical history is unremarkable, no further laboratory or neurologic testing (e.g., computed tomography [CT], positron emission tomography [PET], electroencephalogram [EEG]) are required.
  - e. Psychological and neuropsychological testing are not required for diagnosis but recommended if other academic or developmental concerns are present.<sup>9</sup>
3. **Treatment:** Studies show pharmacologic treatment works best with behavioral treatment as an adjunct.
- a. Before starting a stimulant medication, history should be taken to exclude cardiac symptoms, Wolff-Parkinson-White syndrome, sudden death in the family, hypertrophic cardiomyopathy, and long QT syndrome.<sup>10</sup>
    - (1) See [ADHD Medication Guide](#) for recommended pharmacologic treatments. Also see Table 9-7.

## C. Anxiety Disorders

### 1. Epidemiology:

- a. One of the most common mental health issues that presents in the general pediatric setting. An estimated 15%–20% of children and adolescents are affected, with onset most often before age 25.<sup>11</sup>
- b. Children may develop new anxiety disorders over time and are at higher risk for anxiety and depressive disorders than adults. They are also at risk for social, family, and academic impairments.

### 2. Assessment:

- a. Presentation:
  - (1) May present with fear or worry and not recognize their fear as unreasonable.
  - (2) Commonly have somatic complaints of headache and stomachache
    - (a) Crying, irritability, and angry outbursts are an expression of fear and effort to avoid anxiety-provoking stimulus.

(3) Screening: Pediatric Anxiety Rating Scale (PARS), [SCARED](#), and [Spence Children's Anxiety Scale](#)

3. **Categories:** See DSM-5 for specific criteria for each disorder.<sup>12</sup>

- a. Generalized anxiety disorder
- b. Separation anxiety disorder
- c. Social anxiety disorder
- d. Posttraumatic stress disorder
- e. Obsessive-compulsive disorder
- f. Selective mutism
- g. Specific phobia
- h. Panic disorder
- i. Agoraphobia
- j. Substance/medication-induced anxiety disorder

4. **Treatment:**

a. Best results obtained with a combination of pharmacotherapy ([Table 9-7](#)) and psychotherapy with cognitive-behavioral therapy (CBT).<sup>12</sup>

## **D. Depressive Disorders**

1. **Epidemiology:**

- a. Major depressive disorder: 2% of children, 4%–8% of adolescents
- b. Sub-clinical symptoms: 5%–10% of children
- c. Most common comorbid conditions:
  - (1) Anxiety disorders
  - (2) Disruptive disorders
  - (3) ADHD
  - (4) Substance use (adolescents)

2. **Assessment:**

- a. Major depression:
  - (1) Five or more symptoms for at least 2 weeks, and one of the five must be either depressed/irritable mood or anhedonia.
  - (2) Symptoms cause significant impairment in functioning.
  - (3) Not due to substance use or a medical condition.
  - (4) No history of manic episodes.<sup>13</sup>

3. **Treatment:**

- a. May be initiated in primary care setting or may require a referral depending on severity.
- b. Literature shows that antidepressant medications ([Table 9-7](#)) and CBT combined are the most effective treatment, followed by medication alone, then CBT alone.
- c. Selective serotonin reuptake inhibitors (SSRIs) have a black box warning concerning a possible increase in suicidal thoughts or behaviors in children and adolescents after initiation of medication. Patients should be followed closely for the first 2–4 weeks, then every other week thereafter. SSRIs can be initiated in the primary care setting.<sup>14</sup>
- d. Refer to the Physicians Med Guide prepared by the American Psychological Association (APA) and American Academy of Child

and Adolescent Psychiatry (AACAP) for guidelines regarding medication use for depression in adolescent patients.<sup>14</sup>

## E. Substance Abuse Disorder

### 1. Epidemiology:

- Lifetime diagnosis of alcohol abuse: 0.4%–9%
- Lifetime diagnosis of alcohol dependence: 0.6%–4.3%
- Lifetime diagnosis of drug abuse or dependence: 3.3%–9.8%
- Common comorbid conditions: Disruptive behavior disorders, mood disorders, anxiety disorders

### 2. Assessment (Box 9-1):

- Establish standards of confidentiality.
- CRAFFT Questionnaire (Box 9-2).
- Evaluate for age of onset of use; progression of use for specific substances; circumstances, frequency, and variability of use; and types of agents used.
- Determine treatment goals and readiness for change.
- Toxicology workup should be part of any routine evaluation where substance abuse is concerned.

### 3. Treatment:

- Families should be involved with treatment.
- Medications can be used to manage withdrawal symptoms and/or cravings.

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#### BOX 9-1

##### SIGNS AND SYMPTOMS OF SUBSTANCE ABUSE<sup>15</sup>

- Acute change in mood, behavior, and cognition
- Mood: Depression to euphoria
- Behavior: Disinhibition, lethargy, hyperactivity, agitation, somnolence, and hypervigilance
- Cognition: Impaired concentration, changes in attention span, perceptual and overt disturbances in thinking (e.g., delusions)
- Impairment in psychosocial and academic functioning (family conflict/dysfunction, interpersonal conflict, academic failure)
- Deviant or risk-taking behavior

#### BOX 9-2

##### CRAFFT QUESTIONNAIRE

**C**—Have you ever ridden in a **CAR** driven by someone (or yourself) who was "high" or had been using alcohol or drugs?

**R**—Do you ever use alcohol or drugs to **RELAX**, feel better about yourself, or fit in?

**A**—Do you ever use alcohol/drugs while you are **ALONE**?

**F**—Do your family or **FRIENDS** ever tell you that you should cut down on your drinking or drug use?

**F**—Do you ever **FORGET** things you did while using alcohol or drugs?

**T**—Have you gotten into **TROUBLE** while you were using alcohol or drugs?

**NOTE:** Answering yes to two or more questions is a positive screen.

- c. Treatment of comorbid conditions should occur at the same time.<sup>15</sup>
- d. Find a treatment center at: [www.SAMSHA.org](http://www.SAMSHA.org).

## IX. REFERRAL AND INTERVENTION

### A. State Support

1. **The Individuals with Disabilities Education Act (IDEA)** requires states to provide early intervention services to children.
2. **Early intervention services eligibility criteria vary from state to state.** The National Early Childhood Technical Assistance Center ([www.nectac.org](http://www.nectac.org)) provides information about criteria in each state.

### B. Recommendations

1. **Facilitate communication between family and school.**
2. **Advocate for appropriate services, and regularly monitor their effectiveness.**
3. **Medical workup when indicated.**
4. **Provide pharmacologic intervention as needed.**
5. **Refer to an appropriate specialist when indicated.**

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# Chapter 10

## Endocrinology

*Teresa Mark, MD*

 See additional content on Expert Consult

### I. WEBSITES

Children with Diabetes ([www.childrenwithdiabetes.com](http://www.childrenwithdiabetes.com))

American Diabetes Association ([www.diabetes.org](http://www.diabetes.org))

International Society for Pediatric and Adolescent Diabetes ([www.ispad.org](http://www.ispad.org))

Pediatric Endocrine Society ([www.lwpes.org](http://www.lwpes.org))

### II. DIABETES

#### A. Evaluation and Diagnosis<sup>1-3</sup>

##### 1. Diagnostic criteria (must meet 1 of 4):

- Symptoms for diabetes (polyuria, polydipsia, or weight loss) and random blood glucose  $\geq 200$  mg/dL
- Fasting blood glucose (FPG = no caloric intake for at least 8 hours)  $\geq 126$  mg/dL\*
- Oral glucose tolerance test (OGTT) with a 2-hour postload blood glucose  $\geq 200$  mg/dL\*
- Hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>)  $\geq 6.5\%$

2. **Defining increased risk:** FPG 100–125, 2-hour post OGTT 140–199, HbA<sub>1c</sub> 5.7%–6.4%<sup>†</sup>

3. **Interpreting HbA<sub>1c</sub>:** Estimates average blood glucose for the past 3 months; 6% approximately equals an average of 130 mg/dL, each additional 1%  $\approx$  30 mg/dL more

##### 4. Oral glucose tolerance test:

- Pretest preparation:
  - Calorically adequate diet required for 3 days before the test, with 50% of total calories taken as carbohydrate.
  - Delay test 2 weeks after illness.
  - Discontinue all hyperglycemic and hypoglycemic agents (e.g., salicylates, diuretics, oral contraceptives, phenytoin).
- Procedure: Give 1.75 g/kg (maximum 75 g) oral (PO) glucose after a 12-hour fast, allowing up to 5 minutes for ingestion. Mix glucose with water and lemon juice as a 20% dilution. Quiet activity is permissible during the OGTT. Draw blood samples at 0 and 120 minutes after ingestion.

\*In the absence of symptoms of hyperglycemia, these values should be repeated on another day.

<sup>†</sup>These values are for adults; equivalent values not yet determined in children.

- c. Interpretation: 2-hour blood glucose < 140 mg/dL = normal; 140–199 mg/dL = impaired glucose tolerance;  $\geq 200$  mg/dL = diabetes mellitus (DM).

## B. Diabetes Classification<sup>1,2</sup>

### 1. Type I or type II (most common types, polygenic):

- Patient characteristics (Table 10-1)
- Laboratory characteristics:
  - Islet cell autoantibodies: (GAD-65, insulin, islet cell antibodies) suggestive of type 1. However,  $\approx 15\%$  of children with type 1 diabetes will not have autoantibodies to a specific islet cell antigen and  $\approx 5\%$  will not have any detectable islet cell autoantibodies.  
**NOTE:** Some children with type 2 diabetes will have measurable islet cell autoantibodies.
  - Ketoacidosis: Usually associated with type 1 but does not exclude type 2 (see Sections C and D). Recurrent ketosis, especially diabetic ketoacidosis (DKA), in a type 2 patient should prompt reevaluation of classification.
  - C-peptide: In a type 1 patient, a measurable level >2 years after diagnosis should prompt reevaluation of classification.
  - Insulin and C-peptide: Often unhelpful in initial classification. At presentation, levels usually low in type 1, but there is significant overlap with type 2.

### 2. Other forms of diabetes<sup>4,5</sup>:

- Monogenic diabetes: 1%–2% of DM cases. Due to single-gene mutations, typically relating to insulin production or release. Identifying the gene can have clinical significance.
- Maturity-onset diabetes of youth (MODY):
  - Suspect if autosomal dominant inheritance pattern of early-onset (<25 years) diabetes, insulin independence, absent diabetes mellitus type 2 (DM2) phenotype (nonobese), preservation of C-peptide.
  - Six well-described subtypes: MODY1 and MODY3, which are due to mutations in transcription factors for insulin production, are responsive to sulfonylureas.

TABLE 10-1

#### CHARACTERISTICS SUGGESTIVE OF TYPE 1 VS. TYPE 2 DIABETES AT PRESENTATION

Characteristic	Type 1	Type 2
Onset	Usually prepuberty	Usually postpuberty
Polydipsia and polyuria	Present for days to weeks	Absent or present for weeks to months
Ethnicity	Caucasian	African American, Hispanic, Asian, Native American
Weight	Weight loss	Obese
Other physical findings		Acanthosis nigricans
Family history	Autoimmune diseases	Type 2 diabetes
Ketoacidosis	More common	Less common

- c. Neonatal diabetes (NDM):
  - (1) Defined as DM onset < 6 months of age
  - (2) Rare: 1:160000–260000 live births, typically a *de novo* mutation
  - (3) May be transient (50% recur) or permanent
  - (4) Subset respond to sulfonylureas
- d. Other causes of DM: Diseases of exocrine pancreas due to pancreatitis, trauma, infection, invasive disease (cystic fibrosis [CF], hemochromatosis). Can also be drug or chemically induced.

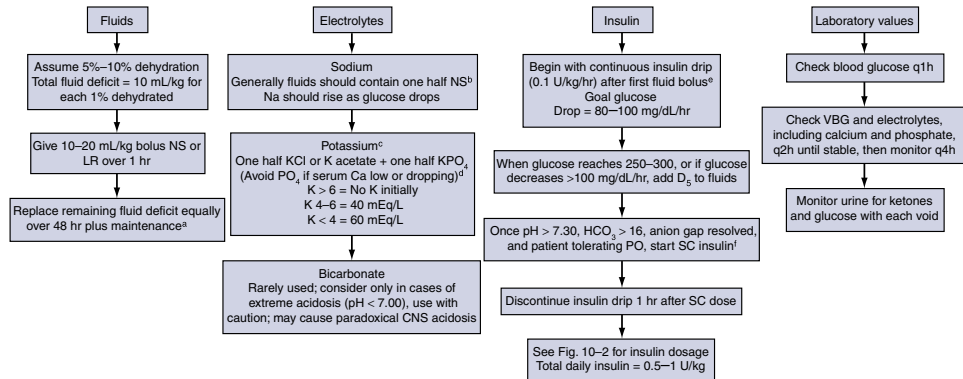
### C. Diabetic Ketoacidosis<sup>6,7</sup>

- 1. **Definition:** Hyperglycemia, ketonemia, ketonuria, and metabolic acidosis (pH < 7.30, bicarbonate < 15 mEq/L)
- 2. **Assessment:**
  - a. History: In *suspected* diabetic, determine whether there is a history of polydipsia, polyuria, polyphagia, weight loss, vomiting, or abdominal pain, as well as history of infection or inciting event. In a *known* diabetic, also determine the usual insulin regimen, timing and amount of last dose.
  - b. Examination: Assess for dehydration, Kussmaul respirations, fruity breath, change in mental status, and current weight.
  - c. Laboratory tests: See Fig. 10-1. Also consider HbA<sub>1c</sub> to assess for chronic hyperglycemia (normal values are 4.5%–5.9%). In a new-onset diabetic, consider islet cell antibodies, insulin antibodies, thyroid antibodies, thyroid function tests, and celiac screen (endomysial antibody or tissue transglutaminase and total immunoglobulin [IgA]).
- 3. **Management:** See Fig. 10-1. Because fluid and electrolyte requirements of patients in DKA vary greatly, the following guidelines are a starting point; therapy must be individualized based on patient dynamics.
  - a. Acidosis: pH is an indicator of insulin deficiency; if acidosis is not resolving, patient may need more insulin. **NOTE:** Initial insulin administration may cause transient worsening of acidosis as potassium is driven into cells in exchange for hydrogen ions.
  - b. Hyperglycemia: Blood glucose is an indicator of hydration status.
- 4. **Cerebral edema:** Most severe complication of DKA. Overly aggressive hydration and rapid correction of hyperglycemia may play a role in its development.
- 5. **Insulin requirements:** Once DKA is resolved, patient will need to be started on a regimen of subcutaneous (SQ) insulin. See Table 10-2 for calculations (also see Table 10-3). Insulin doses are subsequently adjusted based on actual blood sugars. Initially check blood sugars before meals (QAC), at bedtime (QHS), and at 2 AM.

### D. Type II Diabetes Mellitus<sup>8-10</sup>

- 1. **Prevalence:** Increasing among children, especially among African Americans, Hispanics, and Native Americans. Increase is related to increased prevalence of childhood obesity.
- 2. **Etiology:** Abnormality in glucose levels caused by insulin resistance and insulin secretory defect.





<sup>a</sup>Additional fluids may be needed if there is a large negative fluid balance in the first hours of treatment due to the osmotic diuresis when serum glucose is high.

<sup>b</sup>Some DKA protocols recommend using NS rather than half NS during part of the replacement period in an effort to further decrease risk of cerebral edema.

<sup>c</sup>Patients with DKA are total body K<sup>+</sup> depleted and are at risk for severe hypokalemia during DKA therapy. However, serum K<sup>+</sup> levels may be normal or elevated as a result of the shift of K<sup>+</sup> to the extracellular compartment in the setting of acidosis.

<sup>d</sup>Phosphate is depleted in DKA and will drop further with insulin therapy. Consider replacing half of K as KPO<sub>4</sub> for first 8 hr, then all as KCl. Excessive phosphate may induce hypocalcemic tetany.

<sup>e</sup>Lower dose insulin infusions can be considered in very young patients.

<sup>f</sup>Some protocols recommend also waiting for urine ketones to decrease or clear before starting SC insulin.

**FIGURE 10-1**

Management of diabetic ketoacidosis. (Modified from Cooke DW, Plotnick L. Management of diabetic ketoacidosis in children and adolescents. *Pediatr Rev.* 2008;29:431-436.)

**TABLE 10-2**  
**SUBCUTANEOUS INSULIN DOSING**

	Insulin	Dose Calculation	Sample Calculation for 24-kg child	Dose
Total daily dose		0.5–1 unit/kg/day	$0.75 \times 24 = 18$ units/day	18 units
Basal	Glargine OR Detemir	1/2 daily total	$1/2 \ 18 \text{ units} = 9$	9 units
Carbohydrate coverage ratio	Lispro, aspart OR Regular	$450 \div \text{daily total}$ $500 \div \text{daily total}$	$450 \div 18 = 25$	1 unit: 25 g carbohydrate
Correction factor	Lispro, aspart OR Regular	$1800 \div \text{daily total}$ $1500 \div \text{daily total}$	$1800 \div 18 = 100$	1 unit: 100 mg/dL > 120

**TABLE 10-3**  
**CURRENTLY AVAILABLE INSULIN PRODUCTS**

Insulin*	Onset	Peak	Effective Duration
<b>Rapid acting</b> Lispro (Humalog) Aspart (Novo Log) Glulisine (Apidra)	5–15 min	30–90 min	5 hr
<b>Short Acting</b> Regular U100 Regular U500 (concentrated)	30–60 min	2–3 hr	5–8 hr
<b>Intermediate acting</b> Isophane insulin (NPH, Humulin N/Novolin N)	2–4 hr	4–10 hr	10–16 hr
<b>Long acting</b> Glargine (Lantus) Detemir (Levemir)	2–4 hr† Slow	No peak 6–8 hr	20–24 hr 6–24 hr (dose related)
<b>Premixed</b> 70% NPH/30% regular (Humulin 70/30) 75% NPL/25% lispro (Humalog Mix 75/25) 50% NPL/50% lispro (Humalog Mix 50/50) 70% NPA/30% aspart (Novo Log Mix 70/30)	30–60 min 5–15 min 5–15 min 5–15 min	Dual	10–16 hr

\*Assuming 0.1–0.2 U/kg per injection. Onset and duration vary significantly by injection site.

†Time to steady state.

NPA, Insulin aspart protamine (neutral protamine aspart); NPH, neutral protamine Hagedom; NPL, insulin.

Modified from American Diabetes Association. *Practical Insulin: A Handbook for Prescribing Providers*, 2nd ed. Alexandria, Va: American Diabetes Association, 2007.

3. **Presentation:** Although not typical, can present in ketoacidosis (chronic high glucose impairs  $\beta$ -cell function and increases peripheral insulin resistance).
4. **Screening:**
  - a. Consider screening by measuring fasting blood glucose levels in children who are overweight (body mass index > 85th percentile for age and gender) *and* have two of the following risk factors:
    - (1) Family history of type 2 DM in a first- or second-degree relative
    - (2) Race/ethnicity: African American, Native American, Hispanic, or Asian or Pacific Islander
    - (3) Signs associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovarian disease)
  - b. Begin at age 10 years or onset of puberty (whichever occurs first), and repeat every 2 years.
  - c. Based on adult data, HbA<sub>1c</sub> may be used as a screening tool: HbA<sub>1c</sub> = 5.7%–6.4% indicates increased risk of future diabetes; 6.0%–6.5% is abnormal and indicates need for further testing (OGTT, fasting plasma glucose); >6.5% is diagnostic of diabetes.
5. **Treatment:** See Fig. 10-2.

#### E. Monitoring

1. **Glucose control:** Daily blood glucoses; HbA<sub>1c</sub> level every 3 months
2. **Other involved organ systems:** Annual eye examinations and regular screening for hypertension, proteinuria, and hyperlipidemia (monitor Q2 yr with goals of low-density lipoprotein [LDL] < 100 mg/dL, high-density [HDL] > 35 mg/dL, triglycerides [TGs] < 150 mg/dL)

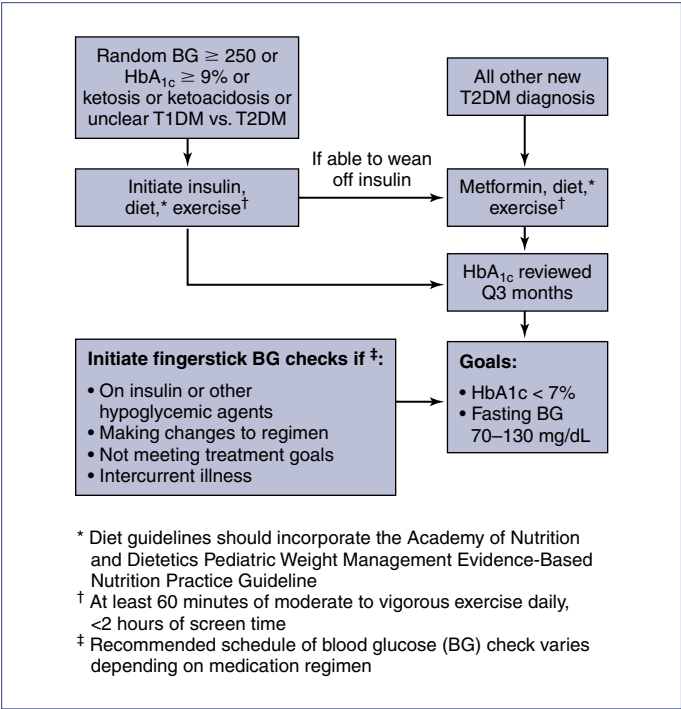
### III. THYROID FUNCTION 10-13

#### A. Thyroid Tests<sup>12,14,15</sup>

1. **Interpretation of thyroid function tests (Table 10-4):** See reference values for age (Table 10-5). Remember that preterm infants have different ranges (Table 10-6).
2. **Thyroid scan:** Used to study thyroid structure and function. Localizes ectopic thyroid tissue and hyperfunctioning and nonfunctioning thyroid nodules.
3. **Technetium uptake:** Measures uptake of technetium by thyroid gland. Levels are increased in Grave's disease and decreased in Hashitoxicosis and hypothyroidism (except dyshormonogenesis, when levels may be increased).

#### B. Hypothyroidism (Table 10-7)

1. **Can be congenital or acquired.** See Table 10-7 for characteristics and types of hypothyroidism.
2. **Hypothyroidism and obesity<sup>16</sup>:** Moderate elevations in thyroid-stimulating hormone (TSH [4–10 mIU/L]), with normal or slightly elevated triiodothyronine (T<sub>3</sub>) and thyroxine (T<sub>4</sub>) are seen in 10%–23% of obese children and adolescents. In these individuals, there does not appear to be a



**FIGURE 10-2**

Treatment decision tree for management of type 2 diabetes (T2DM) in children and adolescents. (Modified from Copeland KC, Silverstein J, Moore KR, et al. Clinical practice guideline: management of newly diagnosed type 2 diabetes mellitus (T2DM) in children and adolescents. Pediatrics. 2013;131:364-382.)

**TABLE 10-4**

**THYROID FUNCTION TESTS: INTERPRETATION**

Disorder	TSH	T <sub>4</sub>	Free T <sub>4</sub>
Primary hyperthyroidism	L	H	High N to H
Primary hypothyroidism	H	L	L
Hypothalamic/pituitary hypothyroidism	L, N, H*	L	L
TBG deficiency	N	L	N
Euthyroid sick syndrome	L, N, H*	L	L to low N
TSH adenoma or pituitary resistance	N to H	H	H
Compensated hypothyroidism†	H	N	N

\*Can be normal, low, or slightly high.

†Treatment may not be necessary.

H, High; L, low; N, normal; T<sub>4</sub>, thyroxine; TBG, thyroxine-binding globulin; TSH, thyroid-stimulating hormone.

TABLE 10-5

AGE-BASED NORMAL VALUES FOR ROUTINE THYROID FUNCTION TESTS<sup>14</sup>

Age	Free T <sub>4</sub> (ng/dL)	TSH (mIU/L)	T <sub>4</sub> (mcg/dL)	T <sub>3</sub> (ng/dL)	Reverse T <sub>3</sub> (ng/dL)	TBG (mcg/mL)
Day of birth	0.94–4.39	2.43–24.3	5.85–18.68	19.53–266.26	19.53–358.70	19.17–44.7
1 wk	0.96–4.08	0.58–5.58*	5.90–18.58	20.83–265.61	19.53–338.52	19.16–44.68
1 mo	1.00–3.44	0.58–5.57*	6.06–18.27	25.39–264.31	19.53–283.84	19.12–44.59
3 mo	1.04–2.86	0.58–5.57*	6.39–17.66	36.46–259.75	19.53–197.90	19.02–44.35
6 mo	1.07–2.44	0.58–5.56*	6.75–17.04	51.43–252.59	19.53–137.36	18.87–44
1 yr	1.10–2.19	0.57–5.54	7.10–16.16	74.87–240.87	18.23–85.93	18.56–43.28
2 yr	1.11–2.05	0.57–5.51	7.16–14.98	103.51–228.50	16.93–55.99	17.94–41.82
5 yr	1.08–1.93	0.56–5.41	6.39–12.94	131.50–212.23	13.02–35.81	16–37.3
8 yr	1.04–1.87	0.55–5.31	5.72–11.71	130.85–202.46	11.72–30.60	14.2–33.09
12 yr	0.99–1.81	0.53–5.16	5.08–10.58	119.78–192.70	11.07–27.99	12.54–29.24
15 yr	1.03–1.77	0.52–5.05	4.84–10.13	110.02–184.88	10.42–27.34	11.96–27.89
18 yr	0.93–1.73	0.51–4.93		101.56–179.03	10.42–26.04	

\*Some labs report the reference range upper limit for TSH for children up to 12 months of age as 8.35 mIU/L.

T<sub>3</sub>, Triiodothyronine; T<sub>4</sub>, thyroxine; TBG, thyroxine-binding globulin; TSH, thyroid-stimulating hormone.

NOTE: If age-specific reference ranges are provided by the laboratory running the assay, please refer to those ranges.

The above ranges are modified from Lem AJ, de Rijke YB, van Toor H, et al. Serum thyroid hormone levels in healthy children from birth to adulthood and in short children born small for gestational age. *J Clin Endocrinol Metab.* 2012;97:3170–3178.

TABLE 10-6

MEAN TSH AND T<sub>4</sub> OF PRETERM AND TERM INFANTS 0–28 DAYS<sup>15</sup>

Age ± SD	Cord (Day 0)	Day 7	Day 14	Day 28
<b>T<sub>4</sub> (mcg/dL)</b>				
23–27*	5.44 ± 2.02	4.04 ± 1.79	4.74 ± 2.56	6.14 ± 2.33
28–30	6.29 ± 2.02	6.29 ± 2.10	6.60 ± 2.25	7.46 ± 2.33
31–34	7.61 ± 2.25	9.40 ± 3.42	9.09 ± 3.57	8.94 ± 2.95
>37	9.17 ± 1.94	12.67 ± 2.87	10.72 ± 1.40	9.71 ± 2.18
<b>FT<sub>4</sub> (ng/dL)</b>				
23–27	1.28 ± 0.41	1.47 ± 0.56	1.45 ± 0.51	1.50 ± 0.43
28–30	1.45 ± 0.43	1.82 ± 0.66	1.65 ± 0.44	1.71 ± 0.43
31–34	1.49 ± 0.33	2.14 ± 0.57	1.96 ± 0.43	1.88 ± 0.46
>37	1.41 ± 0.39	2.70 ± 0.57	2.03 ± 0.28	1.65 ± 0.34
<b>TSH (mIU/L)</b>				
23–27	6.80 ± 2.90	3.50 ± 2.60	3.90 ± 2.70	3.80 ± 4.70
28–30	7.00 ± 3.70	3.60 ± 2.50	4.90 ± 11.2	3.60 ± 2.50
31–34	7.90 ± 5.20	3.60 ± 4.80	3.80 ± 9.30	3.50 ± 3.40
>37	6.70 ± 4.80	2.60 ± 1.80	2.50 ± 2.00	1.80 ± 0.90

\*Weeks gestational age.

FT<sub>4</sub>, Free thyroxine; T<sub>4</sub>, thyroxine; TSH, thyroid-stimulating hormone.

Data modified from Williams FL, Simpson J, Delahunty C, et al. Collaboration from The Scottish Preterm Thyroid Group: Developmental trends in cord and postpartum serum thyroid hormones in preterm infants. *J Clin Endocrinol Metab.* 2004;89:5314–5320.

TABLE 10-7

## HYPOTHYROIDISM

Disease and Clinical Symptoms	Onset	Etiology	Management	Follow-up
<b>PRIMARY/CONGENITAL</b>				
Large fontanelles, lethargy, constipation, hoarse cry, hypotonia, hypothermia, jaundice	<p>Symptoms usually develop within first 2 weeks of life; almost always present by 6 weeks.</p> <p>Some infants may be relatively asymptomatic if the cause is other than absence of the thyroid gland.</p> <p>Treated patients are still at risk for developmental delay.</p>	<p>Primary hypothyroidism: Most common cause is defect of fetal thyroid development. Other causes include TSH receptor mutation or thyroid dysmorphogenesis.</p> <p><i>OR</i></p> <p>Central hypothyroidism: Deficiency of thyrotropin-releasing hormone (TRH) or thyrotropin (TSH).</p>	<p>Goal is to achieve <math>T_4</math> in the upper half of normal range. In primary hypothyroidism, TSH should be kept <math>&lt;5</math>. A minority of infants maintain persistently high TSH despite correction of <math>T_4</math>.</p> <p>Replacement with L-thyroxine as soon as diagnosis is confirmed.</p>	<p>Monitor <math>T_4</math> and TSH at the end of weeks 1 and 2 of therapy and 3–4 weeks after any dose change.</p> <p>If levels are adequate, follow every 1–3 months during the first 12 months.</p>
<b>ACQUIRED</b>				
Growth deceleration; other signs may include coarse, brittle hair, dry, scaly skin, delayed tooth eruption, cold intolerance	Can occur as early as the first 2 years of life.	<p>Hashimoto thyroiditis (diagnosis supported by presence of anti-thyroglobulin or antimicrosomal antibodies).</p> <p>Head/neck radiation.</p> <p>Central hypothyroidism (pituitary/hypothalamic insult).</p>	Replacement with L-thyroxine.	<p>As for primary/congenital.</p> <p>After 2 years, monitor levels every 6–12 months as dose changes become less frequent.</p>

**NOTE:** Thyroid hormone levels in premature infants are lower than those seen in full-term infants. Further, the TSH surge seen at approximately 24 hours of age in full-term babies does not appear in preterm infants. In this population, lower levels are associated with increased illness, but the effect of replacement therapy remains controversial.

L-thyroxine, Levothyroxine; TSH, thyroid-stimulating hormone.

benefit to treating with thyroxine. Values tend to normalize with weight loss, suggesting they are the result, rather than the cause, of obesity in these individuals. Could consider testing for thyroid antibodies to further clarify whether there is true thyroid dysfunction.

3. **Newborn screening for hypothyroidism**<sup>13,17</sup>: Mandated in all 50 states. Measures a combination of TSH and  $T_4$ , based on the particular state's algorithm; 1:25 abnormal tests are confirmed. Congenital hypothyroidism has prevalence of 1:3000–4000 U.S. infants. If abnormal results are found, clinicians should follow recommendations of American College of Medical Genetics—ACT sheets and Algorithm for confirmation testing. See Chapter 13 for further resources on newborn screening.  
**NOTE:** Because of the risk of inducing adrenal crisis if adrenocorticotrophic hormone (ACTH) deficiency is present, *do not* begin treatment of central hypothyroidism until normal ACTH/cortisol function is documented.

## C. Hyperthyroidism

### 1. General:

- a. Symptoms: Hyperactivity, irritability, altered mood, insomnia, heat intolerance, increased sweating, pruritus, tachycardia, palpitations, fatigue, weakness, weight loss despite increased appetite (or weight gain), increased stool frequency, oligomenorrhea or amenorrhea, fine tremor, hyperreflexia, hair loss.
- b. Epidemiology: Prevalence increases with age, beginning in adolescence; 4:1 female-to-male predominance.
- c. Etiology: Most common cause in childhood is Graves disease (see later). Other causes: Subacute thyroiditis, factitious hyperthyroidism (intake of exogenous hormone), TSH-secreting pituitary tumor (rare). Pituitary resistance to thyroid hormone (compensatory rise in  $T_4$ , but TSH remains within normal range).
- d. Laboratory findings:  $\uparrow T_4$ ,  $\uparrow T_3$ , usually  $\downarrow$  TSH. Further tests include TSH receptor–stimulating antibody, thyroid-stimulating immunoglobulin (TSI), antithyroglobulin and antimicrosomal antibodies, free  $T_4$ , and free  $T_3$ .

### 2. Graves disease:

- a. Physical examination: Diffuse goiter, a feeling of grittiness and discomfort in the eye, retrobulbar pressure or pain, eyelid lag or retraction, periorbital edema, chemosis, scleral injection, exophthalmos, extraocular muscle dysfunction, localized dermatopathy, and lymphoid hyperplasia.
- b. Epidemiology: Peak incidence, age 11–15 years; 5:1 female-to-male ratio. Family history of autoimmune thyroid disease.
- c. Etiology: Autoimmune (positive TSI; may also have low titers of thyroglobulin  $\pm$  microsomal antibodies).
- d. Laboratory findings:  $\uparrow T_4$ ,  $\uparrow T_3$ ,  $\downarrow$  TSH ( $\uparrow$  iodine 123 [ $^{123}\text{I}$ ] uptake distinguishes from Hashimoto thyroiditis).
- e. Treatment and monitoring: Methimazole (inhibits formation of thyroid hormone). Propylthiouracil (PTU) should not be used as first-line treatment in children, owing to higher risk of liver dysfunction than with

methimazole. PTU can be considered for those with mild reactions to methimazole. Radioactive iodine ( $^{131}\text{I}$ ) or surgical thyroidectomy are options for initial treatment or refractory cases. Follow symptoms and  $T_4$  and TSH levels.

### 3. **Hashimoto thyroiditis:**

- a. Presentation:  $\pm$  Initial hyperthyroidism, followed by eventual thyroid burnout and hypothyroidism.
- b. Etiology: Autoimmune (significantly elevated thyroglobulin and/or microsomal antibody).
- c. Laboratory findings: Mild to moderate  $\uparrow T_4$  ( $\downarrow^{123}\text{I}$  uptake distinguishes from Graves).
- d. Treatment: Hyperthyroid phase is usually self-limited; patient may eventually need thyroid replacement. Propranolol if symptomatic.

### 4. **Thyroid storm:**

- a. Presentation: Acute onset of hyperthermia, tachycardia, and restlessness. May progress to delirium, coma, and death.
- b. Treatment: Propranolol is used to relieve signs and symptoms of thyrotoxicosis. Potassium iodide may also be used for acute hyperthyroid management. Long-term management as for Graves disease.

### 5. **Neonatal thyrotoxicosis:**

- a. Presentation: Microcephaly, frontal bossing, intrauterine growth retardation (IUGR), tachycardia, systolic hypertension leading to widened pulse pressure, irritability, failure to thrive, exophthalmos, goiter, flushing, vomiting, diarrhea, jaundice, thrombocytopenia, and cardiac failure or arrhythmias. Onset from immediately after birth to weeks.
- b. Etiology: Occurs exclusively in infants born to mothers with Graves disease. Caused by transplacental passage of maternal TSI. Occasionally, mothers are unaware they have Graves. Even if a mother has received definitive treatment (thyroidectomy or radiation therapy), passage of TSI remains possible.
- c. Treatment and monitoring: Propranolol for symptom control. Methimazole to lower thyroxine levels. Digoxin may be indicated for heart failure. Disease usually resolves by age 6 months.

## **IV. PARATHYROID GLAND FUNCTION AND VITAMIN D**

### **A. Parathyroid Gland**

1. **Parathyroid hormone (PTH) function:** Increases serum calcium by increasing bone resorption, increasing calcium and magnesium reuptake in the kidney, increasing phosphorus excretion in the kidney, and increasing 25-hydroxyvitamin D conversion to 1,25-dihydroxyvitamin D in order to increase calcium absorption in the intestine.
2. **Hypoparathyroidism:**
  - a. Presentation: Asymptomatic or mild muscle cramps to hypocalcemic tetany, prolonged QTc, and convulsions.
  - b. Etiology: Results from a decrease in PTH due to decreased function or absence of the parathyroid gland. This can be due to transient



hypoparathyroidism in infants, autoimmune disease, DiGeorge syndrome, iatrogenic removal of the parathyroid gland during other surgical procedures. Pseudohypoparathyroidism results from PTH resistance and is distinguished by normal or elevated PTH.

- c. Laboratory findings: ↓ PTH; ↓ serum  $\text{Ca}^{2+}$ , ↑ serum phosphorus, normal/↓ alkaline phosphatase, ↓ 1,25-OH-vitamin  $\text{D}_3$
  - d. Treatment and monitoring: Calcium supplementation for documented hypocalcemia, vitamin D supplementation with calcitriol. Carefully monitor serum calcium and phosphorus during therapy. Monitor urine calcium levels to avoid hypercalciuria.
- 3. Hyperparathyroidism:**
- a. Presentation: Hypercalcemia leading to vomiting, constipation, abdominal pain, weakness, paresthesias, malaise, and bone pain. Uncommon in childhood.
  - b. Etiology: Primary hyperparathyroidism is uncommon in children and is usually due to overproduction secondary to adenoma or hyperplasia. Adenomas can be associated with multiple endocrine neoplasia (MEN) syndromes (see Expert Consult, [Box EC 10-A](#)). Secondary hyperparathyroidism is more common; develops in response to hypocalcemic states like renal failure or rickets.
  - c. Laboratory findings, primary: ↑ PTH, ↑ serum  $\text{Ca}^{2+}$ ; ↓ serum phosphorus; normal/↑ alkaline phosphatase. In secondary hyperparathyroidism,  $\text{Ca}^{2+}$  normal/↓.
  - d. Treatment for hypercalcemia associated with primary hyperparathyroidism: Hydration is mainstay of treatment; enhances calciuria. Furosemide may be used with caution with adequate hydration. Hydrocortisone (1 mg/kg Q6 hr), reduces intestinal absorption of calcium. Calcitonin transiently opposes bone resorption. In severe hypercalcemia, bisphosphates may be considered. Surgical removal of parathyroid glands (may result in hypoparathyroidism).

## B. Vitamin D Deficiency (Table 10-8)<sup>18-20</sup>

1. **Current recommendations suggest 600 IU/day in children >12 months of age to meet daily requirements.**

**TABLE 10-8**  
**VITAMIN D DEFICIENCY**

Disease, Clinical Symptoms, and Onset	Etiology	Evaluation	Management
<b>Rickets</b> (infancy/childhood): Failure of adequate bone mineralization, leading to soft bones/skeletal deformities	Decreased dietary intake Inadequate exposure to sunlight Increased melanin Impaired renal function	↓ 25-OH vitamin D	Supplementation for: • Breast-fed infants • Those with celiac disease, cystic fibrosis, Crohn's disease, pancreatic deficiency
<b>Osteomalacia</b> (adults): Bone pain and muscle weakness	Fat malabsorption (celiac disease, cystic fibrosis, Crohn's disease)		Repletion per Formulary

## BOX EC 10-A

**MULTIPLE ENDOCRINE NEOPLASIA (MEN) SYNDROMES**

**MEN I:** An autosomal dominant condition characterized by hyperplasia of the endocrine pancreas (which usually secretes gastrin, insulin), the anterior pituitary (prolactin, growth hormone, corticotropin, or non-hormone secreting), and the parathyroid glands. Classified as the presence of two of three of the previously cited benign tumors. Hyperparathyroidism is the most common presenting sign. Although asymptomatic cases require no treatment, proton-pump inhibitors are the mainstay for gastrinomas, and surgery is the treatment of choice for parathyroid tumors. Any tumors in the head of the pancreas should also be removed.

**MEN IIa:** An autosomal dominant condition characterized by hyperplasia or carcinoma of thyroid C cells in association with pheochromocytoma and primary parathyroid hyperplasia. C-cell hyperplasia or tumors usually appear earlier than pheochromocytoma, and hypercalcemia is a late manifestation indicating hyperparathyroidism.

**MEN IIb:** An autosomal dominant syndrome characterized by the occurrence of multiple neuromas in combination with medullary thyroid carcinoma and pheochromocytoma. The neuromas most often occur on mucosal surfaces. Feeding difficulties, poor sucking, diarrhea, constipation, and failure to thrive may begin in infancy or early childhood, many years before the appearance of neuromas or endocrine symptoms.

*For the MEN II family, genetic testing is recommended for all family members. For those who test positive, prophylactic thyroidectomy is universally advised owing to the aggressiveness of medullary thyroid tumors. The ideal age for surgery depends on the particular genetic mutation. Recommended ages range from infancy up into adolescence.*

**TABLE 10-9**

**VITAMIN D, 25-HYDROXYVITAMIN D<sup>18-20</sup>**

25-Hydroxyvitamin D	Value (ng/mL)
Deficiency	<10–15*
Insufficiency	15–20
Optimal level	>20–30†

\*Values <10–15 have been associated with bone changes found in rickets.

†Controversy exists regarding optimal 25-hydroxyvitamin D level. Some experts recommend a level >30 ng/mL as optimal.

Johns Hopkins Laboratory uses 30 ng/mL as cutoff for normal.

**NOTE:** 1,25-Dihydroxyvitamin D is the physiologically active form, but 25-hydroxyvitamin D is the value to monitor for vitamin D deficiency because this approximates body stores of vitamin D. Cutoffs are not yet well defined.

2. **The definition and consequences of vitamin D deficiency and insufficiency is an evolving field.** See [Table 10-9](#) for suggested ranges of 25-hydroxyvitamin D.

**V. ADRENAL FUNCTION<sup>21-23</sup>**

**A. Adrenal Insufficiency**

1. **Etiology:**

- a. Common causes: Congenital adrenal hyperplasia (CAH) and chronic glucocorticoid treatment (suppression of ACTH secretion)
- b. Other causes: Addison disease and hypothalamic or pituitary disease secondary to tumors, surgery, radiation therapy, or congenital defects

2. **Evaluation:**

- a. AM cortisol level (see [Table 10-10](#) for interpretation)
- b. ACTH stimulation test:
  - (1) Purpose: Measures ability of the adrenal gland to produce cortisol in response to ACTH. Most useful in diagnosis of adrenal insufficiency.
  - (2) Interpretation: Normally, a rise in serum cortisol follows ACTH administration. With ACTH deficiency or prolonged adrenal suppression, there is no rise in cortisol after a single ACTH dose. Blunted cortisol response can be indicative of CAH. Lack of response after 3 consecutive days of ACTH stimulation is pathognomonic of Addison disease.
  - (3) Standard-dose ACTH stimulation test (250 mcg intravenously; cortisol measured at 30 minutes. Used to evaluate for primary adrenal insufficiency, although may be used to evaluate for central adrenal insufficiency:
    - (a) For evaluation of primary adrenal insufficiency:
      - <18 mcg/dL: Highly suggestive of adrenal insufficiency
      - >18 mcg/dL: Normal (rules out adrenal insufficiency)
    - (b) For evaluation of central adrenal insufficiency:
      - <16 mcg/dL: Highly suggestive of adrenal insufficiency
      - 16–30 mcg/dL: Adrenal insufficiency less likely but not excluded
      - >30 mcg/dL: Normal (rules out adrenal insufficiency)

- (4) Low-dose ACTH stimulation test (1 mcg/1.73 m<sup>2</sup>); cortisol measured at 30 minutes. Used to evaluate for central adrenal insufficiency, where it may have higher sensitivity than standard-dose test:

Level <16 mcg/dL: Suggestive of adrenal insufficiency

Level 16–22 mcg/dL: Adrenal insufficiency less likely but not excluded

Level >22 mcg/dL: Adrenal insufficiency unlikely

**NOTE:** No test for adrenal insufficiency has perfect sensitivity or specificity, so results must be interpreted in the individual clinical context.

- c. Mineralocorticoid deficiency confirmed with ↑ renin and ↓ aldosterone

### 3. Congenital adrenal hyperplasia<sup>22,23</sup>:

- a. Group of autosomal recessive disorders characterized by a defect in one of the enzymes required in the synthesis of cortisol from cholesterol (Fig. 10-3). Cortisol deficiency results in oversecretion of ACTH and hyperplasia of the adrenal cortex.

TABLE 10-10

#### CORTISOL, 8AM

Interpretation	Cortisol (mcg/dL)
Suggestive of adrenal insufficiency	<5 mcg/dL
Indeterminate	5–14 mcg/dL
Adrenal insufficiency unlikely	>14 mcg/dL

10

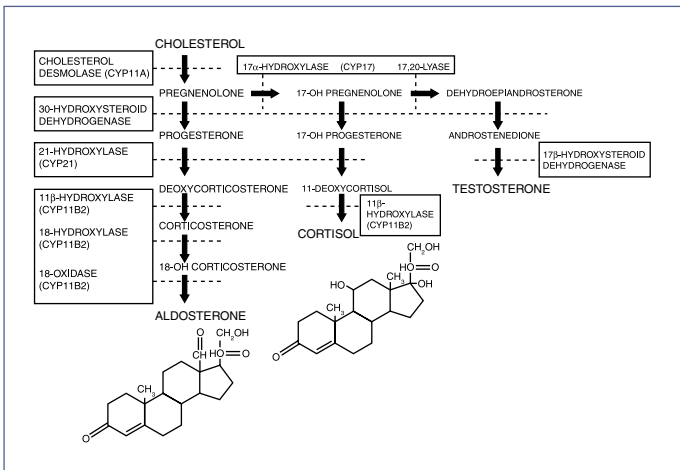


FIGURE 10-3

Biosynthetic pathway for steroid hormones. (From Marshall I, Nimkarn S, New MI. Endocrine hypertension in childhood. Available at [www.endotext.org/pediatrics/pediatrics9/index.html](http://www.endotext.org/pediatrics/pediatrics9/index.html). Accessed December 21, 2007.)

- b. Most common cause of ambiguous genitalia in females.
- c. 21-Hydroxylase deficiency accounts for 90% of cases.
- d. The enzymatic defect results in impaired synthesis of adrenal steroids beyond the enzymatic block and overproduction of the precursors before the block. Two major classifications:
  - (1) Classic (complete enzyme deficiency):
    - (a) Occurs with or without salt loss.
    - (b) Symptoms occur in the absence of stress.
    - (c) Adrenal crisis in untreated patients occurs at 1–2 weeks of life, with signs and symptoms of adrenal insufficiency rarely occurring before 3–4 days of life. (Non–salt-losing forms have a less severe risk for adrenal crisis, owing to preservation of mineralocorticoid synthesis.)
    - (d) Diagnosis: Elevated 17-hydroxyprogesterone (17-OHP) levels (often on newborn screen) (Table 10-11).
    - (e) Elevated testosterone in girls and androstenedione in girls and boys.
    - (f) For apparent male infants presenting with classic CAH, a karyotype should be evaluated to rule out the possibility of a severely masculinized female infant.
  - (2) Nonclassic or simple virilizing form (partial enzyme deficiency):
    - (a) Adrenal insufficiency tends to occur only under stress; manifests as androgen excess after infancy (precocious pubarche, irregular menses, hirsutism, acne, advanced bone age).

**TABLE 10-11**

**17-HYDROXYPROGESTERONE, SERUM**

Age	Baseline (ng/dL)
Premature (31–35 weeks)	≤360
Term infants (3 days)	≤420
1–12 mo	11–170
1–4 yr	4–115
5–9 yr	≤90
10–13 yr	≤169
14–17 yr	16–283
Males, Tanner II–III	12–130
Females, Tanner II–III	18–220
Male, Tanner IV–V	51–190
Females, Tanner IV–V	36–200
Male (18–30 yr)	32–307
Adult female	
Follicular phase	≤185
Midcycle phase	≤225
Luteal phase	≤285

Reference ranges from Quest Diagnostics LC/MS assay (liquid chromatography/tandem mass spectroscopy). For preterm infants or infants born small for gestational age, see Olgemöller B, Roscher AA, Liebl B, et al. Screening for congenital adrenal hyperplasia: adjustment of 17-hydroxyprogesterone cut-off values to both age and birth weight markedly improves the predictive value. *J Clin Endocrinol Metab*. 2003;88:5790–5794.

- (b) Morning 17-OHP levels may be elevated, but diagnosis may require an ACTH stimulation test. A significant rise in the 17-OHP level 60 minutes after ACTH injection is diagnostic. Cortisol response will be decreased.
- (3) Newborn screen:
- Measures 17-OHP on filter paper; can be artificially elevated due to prematurity, sickness, stress; 2% specific, resulting in 98% false-positive rate
  - Results: If 17-OHP 40–100 ng/mL, repeat. If higher, check electrolytes and serum 17-OHP. If K ↑ and Na ↓, initiate treatment with hydrocortisone.
4. **Primary adrenal insufficiency** (Addison disease):<sup>24</sup>
- Syndrome of weakness, fatigue, and hyperpigmentation due to insufficient mineralocorticoid and glucocorticoid production, with compensatory ACTH overproduction. Because of its nonspecific presentation, can be missed in older children.
  - Autoimmune destruction of adrenal glands is the most common cause outside of infancy. In children, it may be part of autoimmune polyendocrine syndrome type 1 (APS-1), which also includes hypoparathyroidism and chronic mucocutaneous candidiasis. Individuals with autoimmune Addison disease should also be screened for other endocrinopathies.
5. **Management of adrenal insufficiency (for relative potency of steroids see Table 10-12)**

TABLE 10-12

**POTENCY OF VARIOUS THERAPEUTIC STEROIDS  
(SET RELATIVE TO POTENCY OF CORTISOL)**

Steroid	Glucocorticoid Effect* (in mg of cortisol per mg of steroid)	Mineralocorticoid Effect† (in mg of cortisol per mg of steroid)
Cortisol (hydrocortisone)	1	1
Cortisone acetate (oral)	0.8	0.8
Cortisone acetate (intramuscular)	0.8	0.8
Prednisone	4	0.25
Prednisolone	4	0.25
Methyl prednisolone	5	0.4
Betamethasone	25	0
Triamcinolone	5	0
Dexamethasone	30	0
9α-fluorocortisone (fludrocortisone)	15	200
Deoxycorticosterone (DOC) acetate	0	20
Aldosterone	0.3	200–1,000

\*To determine cortisol equivalent of a given steroid dose, multiply dose of steroid by corresponding number in column for glucocorticoid or mineralocorticoid effect. To determine dose of a given steroid based on desired cortisol dose, divide desired hydrocortisone dose by corresponding number in the column.

†Total physiologic replacement for salt retention is usually 0.1 mg Flornief, regardless of patient size.

Modified from Sperling MA. *Pediatric Endocrinology*, 3rd ed. Philadelphia: Saunders, 2008:476.

## a. Glucocorticoid maintenance:

- (1) Adrenal insufficiency—replacement of physiologic glucocorticoid production: 6–18 mg/m<sup>2</sup>/day ÷ TID hydrocortisone PO or 1.5–3.5 mg/m<sup>2</sup>/day prednisone ÷ BID (or equivalent glucocorticoid dose of another steroid). Typically, lower doses are required for central adrenal insufficiency, intermediate doses for primary adrenal insufficiency, and higher doses for CAH. Consultation with an endocrinologist is recommended.
- (2) Doses are often titrated to preserve normal skeletal growth and rate of skeletal maturation, and in CAH to suppress production of excess androgen.

## b. Mineralocorticoid maintenance:

- (1) These patients should have ready access to salt.
- (2) For salt-losing forms of adrenal insufficiency (e.g., CAH, Addison disease): 0.1 mg/m<sup>2</sup>/day (typical range: 0.05–0.15 mg) oral (PO) fludrocortisone acetate once daily is recommended. (**NOTE:** Intravenous [IV] hydrocortisone at 50 mg/m<sup>2</sup>/day will supply a maintenance amount of mineralocorticoid activity. Synthetic steroids such as prednisone and dexamethasone do not supply appropriate mineralocorticoid effects.)
- (3) Infants also require 1–2 g (17–34 mEq) of sodium supplementation per day.
- (4) Always monitor blood pressure and electrolytes when supplementing mineralocorticoids.

## c. Stress-dose glucocorticoids:

- (1) Glucocorticoid dosage should increase in patients with fever or other illness to mimic normal physiologic cortisol response to stress.
- (2) Minor ambulatory illness stress dose: 30–50 mg/m<sup>2</sup>/day of hydrocortisone PO ÷ TID or 6–10 mg/m<sup>2</sup>/day prednisone PO ÷ BID.
- (3) Major stress (surgery/severe illness/adrenal crisis): Hydrocortisone 50 mg/m<sup>2</sup> IV bolus, then 25–100 mg/m<sup>2</sup>/day IV (as a continuous infusion) or intramuscular (IM) injection of 25 mg/m<sup>2</sup>/dose Q6 hr

6. **Acute adrenal crisis:**

- a. Often precipitated by acute illness, trauma, surgery, or exposure to excess heat.
- b. Presentation: Emesis, diarrhea, dehydration, hypotension, metabolic acidosis, shock.
- c. Laboratory values: Often hypoglycemia, hyponatremia, and hyperkalemia. In addition, serum cortisol and aldosterone are decreased, and ACTH and renin are elevated. In infants with CAH, 17-OHP is increased. **NOTE:** Performing these studies before steroid administration is useful to confirm the diagnosis, but treatment should not be delayed.
- d. Management includes rapid volume expansion to support blood pressure, sufficient dextrose to maintain blood glucose, close monitoring of electrolytes, and corticosteroid administration.
  - (1) Give 50 mg/m<sup>2</sup> of hydrocortisone by IV bolus (rapid estimate: infants = 25 mg; children = 50–100 mg), followed by 50 mg/m<sup>2</sup>/24 hr by continuous drip (preferable) or divided Q3–4 hr.

- (2) Hydrocortisone and cortisone are the only glucocorticoids that provide the necessary mineralocorticoid effects.

### 7. Cushing syndrome:<sup>25</sup>

- a. Signs and symptoms (including rapid weight gain with central obesity, buffalo hump, moon face, striae, thinning of skin and other membranes, hypertension) associated with elevated cortisol levels and overexposure to glucocorticoids (either endogenous or exogenous). Relatively rare in children, with most cases resulting from iatrogenic causes.
- b. Cushing evaluation:
  - (1) 24-hour urine collection for excess cortisol (normal value range by mass spectrometry:  $\leq 27\text{--}30$  ng/mL).
  - (2) Salivary cortisol level: Measured at 11 PM (*spit in a tube*); levels are akin to free serum cortisol. Normal range is  $<0.2$  mcg/dL.
  - (3) Dexamethasone suppression test:
    - (a) Dexamethasone suppresses secretion of ACTH by the normal pituitary, decreasing endogenous production of cortisol. Useful in determining the etiology of glucocorticoid or androgen overproduction.
    - (b) Overnight dexamethasone suppression test: Measure serum cortisol at 8 AM; preceded by 1 mg of dexamethasone PO given at 11 PM the night before. Level  $<1.8$  mcg/dL (50 nmol/L) is within normal range of suppression.

**NOTE:** Random cortisol is not useful in evaluation for Cushing syndrome.

### B. Adrenal Medulla—Pheochromocytoma<sup>26-28</sup>

1. **Pheochromocytoma only accounts for  $\approx 1\%$  of pediatric hypertension.** Often associated with syndromes: MEN IIa and IIb, Von Hippel-Lindau, neurofibromatosis (NF)1, familial paraganglioma syndrome.
2. **Evaluation for pheochromocytoma should involve imaging and laboratory workup.** See Expert Consult, Chapter 10, for additional information about plasma concentrations of free, fractionated metanephrines.
3. **Measurement of free, fractionated metanephrines in plasma:**
  - a. Use: Detection of pheochromocytoma
  - b. Upper limits of normal: Somewhat assay dependent
    - (1) One study suggests upper normal limits to be metanephrines, 0.3 nmol/L; normetanephrines, 0.6 nmol/L.<sup>27</sup>
    - (2) A pediatric study suggests metanephrines for boys, 0.52; girls, 0.37 nmol/L; normetanephrines for boys, 0.53; girls, 0.42 nmol/L.<sup>28</sup>

## VI. POSTERIOR PITUITARY GLAND—VASOPRESSIN<sup>29</sup>

### A. Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH)

1. **Presentation:** Hyponatremia ( $\text{Na}^+ < 135$  mEq/L) with inappropriately concentrated urine in the setting of euvolemia or mild hypervolemia
2. **Etiology:** Central nervous system (CNS) trauma, CNS infection, CNS or other types of surgery, particularly tonsillectomy and adenoidectomy, pneumonia



3. **Laboratory findings:** ↓ serum  $\text{Na}^+$  and  $\text{Cl}^-$  with normal  $\text{HCO}_3^-$ , hypouricemia, inappropriately concentrated urine
4. **Treatment:** Correct hyponatremia slowly with fluid restriction ( $\approx 10\%$  rise in  $\text{Na}^+$  per 24 hours). *In the setting of coma or seizures*, use hypertonic saline to rapidly correct  $\text{Na}^+$  to  $\approx 120\text{--}125$  mEq/L. Definitive therapy: identify and treat the underlying cause

## B. Diabetes Insipidus (DI)<sup>23</sup>

1. **General:** Inability to concentrate urine
- a. Presentation: Infants may present with failure to thrive, vomiting, constipation, unexplained fevers. In more severe cases, severe dehydration, hypovolemic shock, and seizure may occur.
- b. Etiology: May be central or nephrogenic (see below).
- c. Diagnosis: Water deprivation test. Vasopressin test differentiates between central and nephrogenic DI.
  - (1) Water deprivation test:
    - (a) Purpose: Determines ability to concentrate urine; useful in diagnosis of DI. Risk of dehydration and hypernatremia, so careful supervision is required.
    - (b) Method:
      - (i) Begin test after a 24-hour period of adequate hydration and stable weight.
      - (ii) Obtain a baseline weight after bladder emptying.
      - (iii) Restrict fluids. Measure body weight and urine specific gravity and volume hourly.
      - (iv) Check serum  $\text{Na}$  and urine and serum osmolality Q2 hr. (Hematocrit and blood urea nitrogen [BUN] levels may also be obtained but are not critical.) Monitor carefully to ensure fluids are not ingested during the test.
      - (v) Terminate test if weight loss approaches 5%.
    - (c) Interpretation:
      - (i) Normal individuals and those with psychogenic DI: Urine will be concentrated to 500–1400 mOsm/L; plasma osmolality will be 288–291 mOsm/L. Urine specific gravity rises to at least 1.010, urine-to-plasma osmolality ratio is  $>2$ , urine volume decreases significantly, and there should be no appreciable weight loss. Urine osmolality  $> 1000$  mOsm/L (or  $> 600$  mOsm/L for  $>1$  hour) generally excludes a diagnosis of DI.
      - (ii) Central or nephrogenic DI: Specific gravity remains  $< 1.005$ . Urine osmolality remains  $< 150$  mOsm/L, with no significant reduction of urine volume. Weight loss of up to 5% usually occurs. At the end of the test, serum osmolality  $> 290$  mOsm/L,  $\text{Na} > 150$  mEq/L, and a rise of BUN and hematocrit provide evidence the patient has DI.
  - (2) Vasopressin test:
    - (a) Purpose: Used to differentiate between central (ADH-deficient) and nephrogenic DI

- (b) Method: Vasopressin given subcutaneously ( $1 \text{ U/m}^2$ ), preferably at the end of water deprivation test. Urine output, urine specific gravity, and water intake are monitored.
- (c) Interpretation:
  - (i) Central DI: Patients concentrate their urine ( $>1.010$ ), demonstrate a reduction of urine volume and decreased fluid intake in response to exogenous vasopressin
  - (ii) Nephrogenic DI: No significant change in fluid intake, urine volume, or specific gravity
  - (iii) Psychogenic DI: Continued fluid intake, decreased urine output, and increased specific gravity

## 2. Central DI:

- a. Etiology: Caused by vasopressin deficiency, associated with CNS injury, including trauma and tumors. After trauma to axons of vasopressin-containing neurons, a temporary or permanent DI may result. Owing to the initial edema occurring in the area of the hypothalamus and pituitary, a short-lived period (2–5 days) of DI is observed. This is succeeded by a stage of SIADH as dying neurons release vasopressin. The final stage results in permanent DI if a significant number of neurons are injured.
- b. Laboratory findings: Low urine specific gravity ( $<1.005$ ), low urine osmolality (50–200), low vasopressin ( $<0.5 \text{ pg/mL}$ )
- c. Treatment: IV, PO, SQ, or nasal desmopressin acetate (DDAVP); titrate dosage to urine output. Goal is  $\geq 1$ -hour period of diuresis per day that stimulates thirst. Monitor electrolytes. Infants are often not treated with DDAVP because of difficulty monitoring input and output. Rather, they can be treated with increased free water and salt restriction.

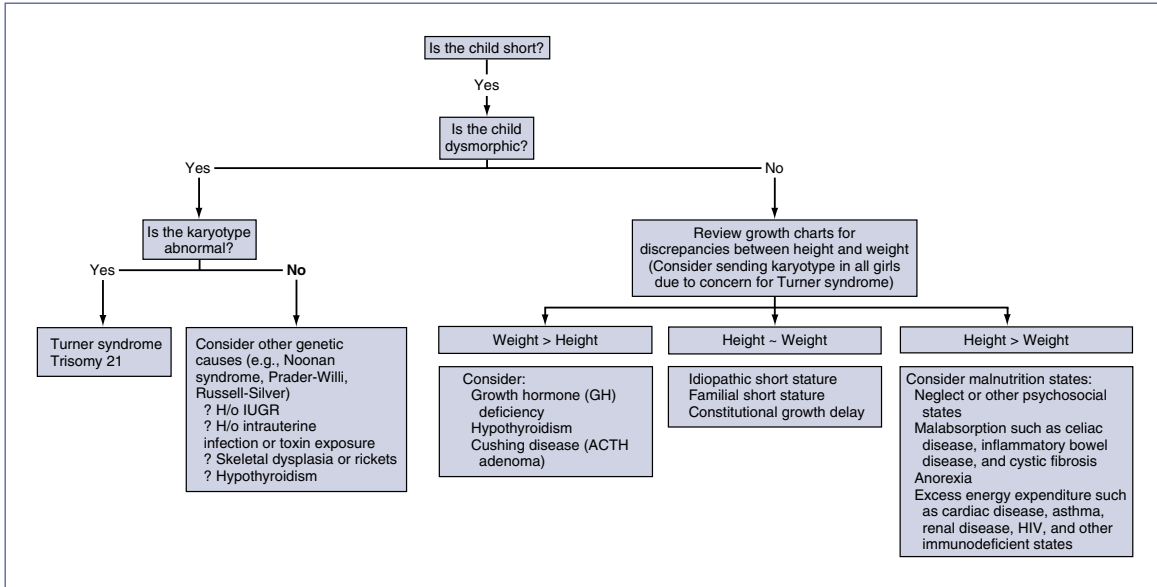
## 3. Nephrogenic DI:

- a. Etiology: Caused by renal tubular resistance to vasopressin; genetic or acquired
- b. Laboratory findings: Low urine specific gravity ( $<1.005$ ), low urine osmolality (50–200 mOsm/L)
- c. Treatment: Increase free water and a low-salt diet

## VII. GROWTH AND SEXUAL DEVELOPMENT 233

### A. Growth

- 1. **Target height range:** Calculated as midparental stature  $\pm 2 \text{ SD}$  (1 SD = 2 inches)
  - a. Midparental stature for boys:  $(\text{Paternal height} + \text{maternal height} + 5 \text{ inches})/2$
  - b. Midparental stature for girls:  $(\text{Paternal height} + \text{maternal height} - 5 \text{ inches})/2$
- 2. **Short stature (Fig. 10-4):**
  - a. Definition: Height less than 3rd percentile, decreasing growth velocity, height percentile below target height range.
  - b. Differential diagnosis: Constitutional growth delay (CGD) and familial short stature (FSS) must be distinguished from pathologic causes of short stature.

**FIGURE 10-4**

Differential diagnosis of short stature.

- (1) FSS: Characterized by slow growth rate during the first 2–3 years of life, followed by a low-normal growth velocity. Bone age x-rays may be within normal limits for age.
  - (2) CGD: Typically characterized by similar growth charts as those with FSS, but a delay in onset of puberty and skeletal maturation allows for a period of catch-up growth. Family history of delayed puberty is often present. Bone age x-rays may be delayed for age.
  - (3) Pathologic short stature (see Fig. 10-4).
- c. Initial evaluation: Detailed history/physical examination, evaluation of growth curves and pubertal stage. Initial screening tests include complete blood cell count (CBC), liver function tests, electrolytes, erythrocyte sedimentation rate, and urinalysis (including pH and specific gravity). Also consider thyroid function tests, serum insulin-like growth factor (IGF)-1 (Table 10-13) and IGF-binding protein-3 (IGFBP-3), tissue transglutaminase for celiac disease, bone age (radiograph of left wrist and hand), and karyotype (in girls). Consider a skeletal survey in a patient with disproportionate features.
3. **Tall stature:** Most common cause is familial tall stature or precocious puberty. Bone age may be helpful.
  4. **Obesity:** A growing problem in pediatric population. Although the majority do not have endocrine etiology, two disease categories may be addressed when approaching the obese patient:
    - a. Hypothyroidism: May be evaluated with serum thyroid function tests

TABLE 10-13

## INSULIN-LIKE GROWTH FACTOR 1 (IGF-1)

Age (years)	Male (ng/mL)	Females (ng/mL)
<1	≤142	≤185
1–1.9	≤134	≤175
2–2.9	≤135	≤178
3–3.9	30–155	38–214
4–4.9	28–181	34–238
5–5.9	31–214	37–272
6–6.9	38–253	45–316
7–7.9	48–298	58–367
8–8.9	62–347	76–424
9–9.9	80–398	99–483
10–10.9	100–449	125–541
11–11.9	123–497	152–593
12–12.9	146–541	178–636
13–13.9	168–576	200–664
14–14.9	187–599	214–673
15–15.9	201–609	218–659
16–16.9	209–602	208–619
17–17.9	207–576	185–551

**NOTE:** A clearly normal IGF-1 level argues against growth hormone (GH) deficiency, except in young children, where there is considerable overlap between normals and those with GH deficiency.

Reference ranges from Quest Diagnostics LC/MS (liquid chromatography/tandem mass spectrometry) assay.

- b. Cushing syndrome: Unlikely without linear growth failure in addition to obesity (see Section V for laboratory testing details)
- 5. **Polycystic ovarian syndrome (PCOS):**
  - a. Syndrome of hyperandrogenism and menstrual dysfunction
  - b. Diagnostic criteria:
    - (1) Hyperandrogenism: Clinical characteristics are hirsutism, acne, and female pattern alopecia. Biochemical characteristic is elevated free testosterone, calculated from total serum testosterone and sex hormone binding protein (SHBG).
    - (2) Menstrual dysfunction: Amenorrhea or oligomenorrhea.
    - (3) Polycystic ovaries: Ultrasound (US) characteristics are increased ovarian volume (reliable in adolescents via transabdominal US) or follicular phase with  $\geq 12$  follicles measuring 2–9 mm (reliable via transvaginal US only).
  - c. Management:
    - (1) Weight reduction and other lifestyle changes increase SHBG (thus decreasing free testosterone) can restore ovulation, and increase insulin sensitivity.
    - (2) Treatment of hirsutism/acne: Hormonal contraceptives.
    - (3) Insulin-sensitizing agents (e.g., metformin) may help mitigate metabolic consequences.
    - (4) Prevention of endometrial hyperplasia (increased risk of endometrial cancer) by intermittent induction of menstruation or prevention of endometrial proliferation by hormonal contraception.

## B. Sexual Development

- 1. **Delayed puberty:** For girls, no pubertal development by age 14 years, or >5 years between thelarche and adrenarche. Primary amenorrhea: no menarche by age 16 years in the presence of secondary sexual characteristics, or no menarche and no secondary sexual characteristics by age 14 years. For boys, no testicular enlargement by age 14 years, or >5 year for genital development.
- a. Delayed puberty may be divided according to luteinizing hormone (LH) (Table 10-14) and follicle-stimulating hormone (FSH) levels (Table 10-15):
  - (1) **Hypergonadotropic hypogonadism** (high LH and FSH): Primary gonadal failure, possibly due to Turner or Klinefelter syndromes, androgen insensitivity, tumor, chemotherapy.
  - (2) **Hypogonadotropic hypogonadism** (low or normal LH/FSH): May be due to constitutional delay or central gonadotropin deficiency. Of the latter cause, etiologies include Kallman syndrome (most common cause of isolated gonadotropin deficiency), CNS tumors, hypopituitarism.
- b. Evaluation of delayed puberty may also be divided into the following categories (Fig. 10-5):
  - (1) Constitutional delay
  - (2) Hypopituitarism
  - (3) Chromosomal abnormality

TABLE 10-14

## LUTEINIZING HORMONE

Age	Males (mIU/mL)	Females (mIU/mL)
0–2 yr	Not established	Not established
3–7 yr	≤0.26	≤0.26
8–9 yr	≤0.46	≤0.69
10–11 yr	≤3.13	≤4.38
12–14 yr	0.23–4.41	0.04–10.80
15–17 yr	0.29–4.77	0.97–14.70
Tanner Stages	Males (mIU/mL)	Females (mIU/mL)
I	≤0.52	≤0.15
II	≤1.76	≤2.91
III	≤4.06	≤7.01
IV–V	0.06–4.77	0.10–14.70

Reference values are from Quest Diagnostics immunoassay. For more information visit [www.questdiagnostics.com](http://www.questdiagnostics.com).

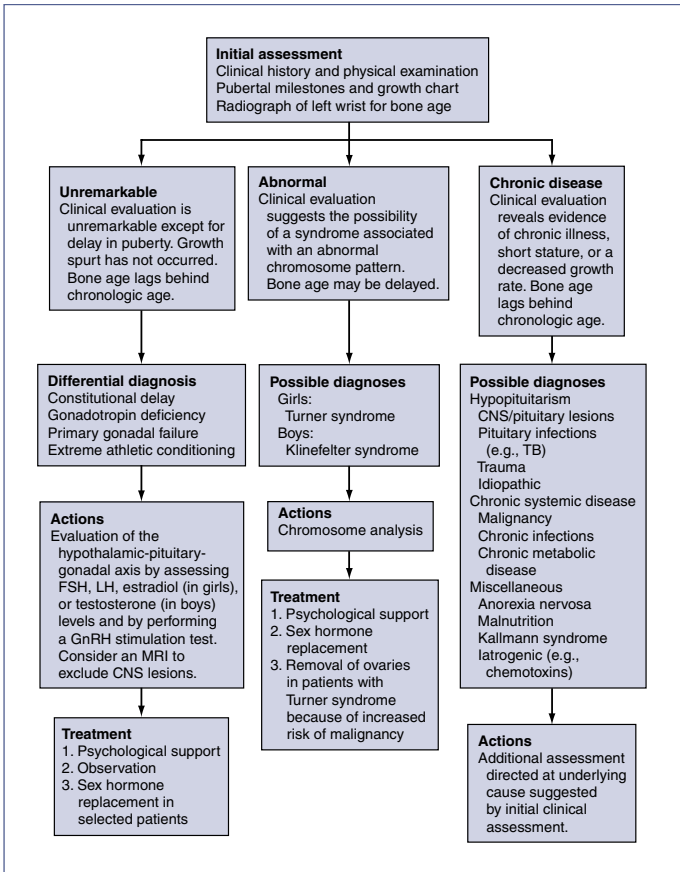
TABLE 10-15

## FOLLICLE-STIMULATING HORMONE

Age	Male (mIU/mL)	Female (mIU/mL)
0–4 yr	Not established	Not established
5–9 yr	0.21–4.33	0.72–5.33
10–13 yr	0.53–4.92	0.87–9.16
14–17 yr	0.85–8.74	0.64–10.98

Reference values are from Quest Diagnostics immunoassay. For more information visit [www.questdiagnostics.com](http://www.questdiagnostics.com).

- c. Initial evaluation: LH and FSH, bone age, and thyroid studies. A gonadotropin-releasing hormone (GnRH) stimulation test can be obtained to rule out hypogonadotropic hypogonadism.
- d. GnRH stimulation test:<sup>39</sup>
  - (1) Measures pituitary luteinizing hormone (LH) and FSH reserve: Helpful in the differential diagnosis of precocious or delayed sexual development.
  - (2) Method: Give 20 mcg/kg GnRH analog (Leuprolide) SQ, and measure LH and FSH levels at 0 and 60 minutes.
  - (3) Interpretation: Prepubertal children should show no or minimal increase in LH and FSH in response to GnRH. A rise of LH to > 3.3–5.0 IU/L is evidence of central puberty.
2. **Precocious puberty:** Traditionally defined as any sign of secondary sexual maturation before age 8 years in girls and age 9 years in boys. More recent data suggest early puberty may not warrant extensive evaluation or intervention if it occurs after age 6 years in African-American girls or after age 7 years in Caucasian girls.

**FIGURE 10-5**

An approach to the child presenting with delayed puberty. CNS, Central nervous system; FSH, follicle-stimulating hormone; GnRH, gonadotropin-releasing hormone; LH, luteinizing hormone; MRI, magnetic resonance imaging; TB, tuberculosis.<sup>37</sup> (From Blondell R, Foster MB, Dave KC. *Disorders of puberty*. Am Family Phys. 1999;60: 209-218.)

- a. Central, true, isosexual, or complete precocious puberty (CPP): Involves premature activation of hypothalamic-pituitary-gonadal axis, leading to increased GnRH and therefore increased LH/FSH; five times more likely to occur in females and often represents an idiopathic variant of normal puberty. In the majority of males with CPP, a CNS insult or structural anomaly is the cause.

TABLE 10-16

## ESTRADIOL

Age	Level (pg/mL)
Prepubertal children	<25
Men	6–44
Women	
Luteal phase	26–165
Follicular phase	None detected–266
Midcycle	118–355
Adult women on OCP	None detected–102

NOTE: Normal infants have elevated estradiol at birth, which decreases to prepubertal values during the first week of life.

Estradiol levels increase again between age 1 and 2 months and return to prepubertal values by age 6–12 months.

OCP, Oral contraceptive pill.

Values from JHH Laboratories.

- b. Peripheral or pseudoprecocious puberty: GnRH-independent puberty; involves adrenal, gonadal, ectopic, or exogenous sources of hormone production. Most common causes are CAH, adrenal tumors, McCune-Albright syndrome, gonadal tumors, human chorionic gonadotropin (hCG)-producing tumors, and exogenous sex hormones. Hypothyroidism can also cause GnRH-independent precocity. Penile length is disproportionately greater than testicular size in pseudo-precocious puberty, whereas testicular volume is disproportionately greater than penile size in normal puberty and CPP.
- c. Initial evaluation: Begin with history (assessing for premature thelarche/adrenarche) physical examination, and growth curves.
  - (1) Bone age (generally >2 years in advance of chronologic age in long-standing precocious puberty due to action of sex hormones)
  - (2) Assess degree of estrogenization or virilization: Check plasma estradiol or plasma testosterone/dehydroepiandrosterone (DHEAS), respectively. Check basal and/or GnRH-stimulated LH levels (see Table 10-14), estradiol measurement in girls (Table 10-16), testosterone levels in boys (Tables 10-17 and 10-18), 17-OHP levels (Table 10-11), DHEA levels (Tables 10-19 and 10-20), and urinary 17-ketosteroids.
  - (3) Imaging: Magnetic resonance imaging (MRI) of the brain may help identify a CNS lesion. In girls, pelvic ultrasonography may identify ovarian cysts, whereas in boys it may detect nonpalpable Leydig-cell tumors and should be considered in cases of asymmetric testicular volume or peripheral precocious puberty. For normal testicular size and volume see Table 10-21.

### 3. Ambiguous genitalia:

- a. Clinical findings in a neonate suspicious for ambiguous genitalia: Anogenital ratio > 0.5 (distance between anus and posterior fourchette divided by distance between anus and base of clitoris), phallus length < 1.9 cm (mean newborn length: 2.5 SD), clitoromegaly (length > 1 cm), nonpalpable gonads in an apparent male, and hypospadias associated with separation of scrotal sacs or undescended testis.



**TABLE 10-17**

**TESTOSTERONE, TOTAL SERUM**

Age	Male (ng/dL)	Female (ng/dL)
Cord blood	17–61	16–44
1–10 days	≤187	≤24
1–3 mo	72–344	≤17
3–5 mo	≤201	≤12
5–7 mo	≤59	≤13
7–12 mo	≤16	≤11
1–5.9 yr	≤5	≤8
6–7.9 yr	≤25	≤20
8–10.9 yr	≤42	≤35
11–11.9 yr	≤260	≤40
12–13.9 yr	≤420	≤40
14–17.9 yr	≤1000	≤40
≥18 (adult)	250–1100	2–45
<b>Tanner Stage</b>		
Stage I	≤5	≤8
Stage II	≤167	≤24
Stage III	21–719	≤28
Stage IV	25–912	≤31
Stage V	110–975	≤33

**NOTE:** Normal testosterone/dihydrotestosterone (T/DHT) ratio is <18 in adults and older children, <10 in neonates. T/DHT ratio >20 suggests 5- $\alpha$ -reductase deficiency or androgen insensitivity syndrome.

Reference ranges from Quest Diagnostics LC/MS (liquid chromatography/tandem mass spectrometry) assay.

**TABLE 10-18**

**TESTOSTERONE, FREE**

Age	Male (pg/mL)	Female (pg/mL)
5.9–9 yr	≤5.3	0.2–5.0
10–13.9 yr	0.7–52	0.1–7.4
14–17.9 yr	18–111	0.5–3.9
18–69 yr	35–155	0.1–6.4

Reference ranges from Quest Diagnostics LC/MS (liquid chromatography/tandem mass spectrometry) assay.

**TABLE 10-19**

**DEHYDROEPIANDROSTERONE (DHEA), UNCONJUGATED**

Age	ng/dL
1–5 yr	≤377
6–9 yr	19–592
10–13 yr	42–1067
14–17 yr	137–1489
Adult male	61–1636
Adult female	102–1185

Reference ranges from Quest Diagnostics LC/MS (liquid chromatography/tandem mass spectrometry) assay.

TABLE 10-20

## DEHYDROEPIANDROSTERONE SULFATE (DHEA-S)

Age	Male (mcg/dL)	Female (mcg/dL)
<1 mo	≤316	15–261
1–6 mo	≤58	≤74
7–11 mo	≤26	≤26
1–3 yr	≤15	≤22
4–6 yr	≤27	≤34
7–9 yr	≤91	≤92
10–13 yr	≤138	≤148
14–17 yr	38–340	37–307
<b>Tanner Stages (ages 7–17)</b>		
I	≤49	≤46
II	≤81	15–133
III	22–126	42–126
IV	33–177	42–241
V	110–370	45–320

Reference values from Quest Diagnostics assay. For more information see [www.questdiagnostics.com](http://www.questdiagnostics.com).

TABLE 10-21

## TESTICULAR SIZE

Tanner Stage (Genital)	Length (cm) (Mean ± SD)	Volume (mL)
I	2.0 ± 0.5	2
II	2.7 ± 0.7	5
III	3.4 ± 0.8	10
IV	4.1 ± 1.0	20
V	5.0 ± 0.5	29

NOTE: Testicular volume of >4 mL or a long axis >2.5 cm is evidence that pubertal testicular growth has begun.  
SD, Standard deviation.

- b. Etiology: Most common cause is CAH (see [Section IV.A.3](#)). Other causes: testicular regression syndrome, androgen insensitivity, testosterone biosynthesis disorders, and chromosomal abnormalities.
- c. Diagnosis: Based on karyotype, measurement of gonadotropins (LH, FSH), adrenal steroids (cortisol, 17-OHP, and ACTH stimulation test), testosterone precursors (DHEA, androstenedione), testosterone, dihydrotestosterone (DHT), and hCG stimulation test (see hCG stimulation test on Expert Consult). **NOTE:** Best test for 5- $\alpha$ -reductase deficiency is the testosterone-to-DHT ratio.
- d. **Cryptorchidism:**
  - (1) Prevalence: 3% of term male infants. About 50% of cryptorchid testicles descend by age 3 months and 80% by 12 months. Neoplasm occurs in 48.9% of individuals with untreated cryptorchidism, and 25% of those tumors occur in the contralateral testis.

- (2) Evaluation: Rule out virilized female with a karyotype. hCG stimulation test can be used to differentiate cryptorchidism from anorchia. Human chorionic gonadotropin (hCG) stimulation test:
  - (a) Measures capacity for testosterone biosynthesis; useful in differentiation of cryptorchidism (undescended testes) from anorchia (absent testes).
  - (b) Method: Give 1000 units of intravenous (IV) or intramuscular (IM) hCG for 3 days, and measure serum testosterone and dihydrotestosterone on day 0 and day 4.
  - (c) Interpretation: Testosterone level  $>100$  ng/dL in response to hCG stimulation is evidence for adequate testosterone biosynthesis. In cryptorchidism, testosterone rises to adult levels after hCG administration; in anorchia, there is no rise.
- (3) Treatment: Removal of trapped testicle at 1 year of life.

### VIII. NEONATAL HYPOGLYCEMIA EVALUATION<sup>40</sup>

#### A. Neonatal Hypoglycemia and Glucagon Stimulation Test<sup>40</sup>

1. **Definition of hypoglycemia:** Serum glucose level insufficient to meet metabolic requirements; can vary with perinatal stress, birth weight, and maternal factors. For practical purposes, value is defined as  $<45$  mg/dL. **NOTE:** Bedside glucometer is inaccurate at levels  $<40$  mg/dL; stat serum glucose must be sent.
2. **Symptoms:** Abnormal cry, seizures, apnea, hypotonia, bradycardia, hypothermia.
3. **Treatment:** Do not delay while awaiting serum glucose results:
  - a. Plasma glucose 25–45 mg/dL (1.4–2.5 mM), asymptomatic: breast feed or nipple/gavage with formula
  - b. Plasma glucose level  $<25$  mg/dL ( $<1.4$  mM)  $\pm$  symptoms, asymptomatic infants who do not tolerate enteral feeding, or symptomatic infants:
    - (1) Give IV bolus of glucose 0.25 g/kg (2.5 mL/kg of 10% glucose, or 1 mL/kg of 25% glucose) over 1–2 minutes.
    - (2) Continue IV glucose at a rate of 6–8 mg/kg/min (3.6–4.8 mL/kg/hr of 10% glucose).
    - (3) Monitor blood glucose Q30–60 min, and increase glucose delivery by 1–2 mg/kg/min if blood glucose is consistently  $<50$  mg/dL.
4. **If serum glucose is consistently  $<45$  mg/dL:** Further endocrine workup warranted. At the time of hypoglycemia (serum glucose  $<45$  mg/dL), obtain serum levels of glucose, insulin, growth hormone, free fatty acids, and  $\beta$ -hydroxybutyrate.
5. **Glucagon stimulation test:** At the time of hypoglycemia, obtain above laboratory tests, administer glucagon, and obtain serum glucose levels Q10 min  $\times$  4. Repeat growth hormone and cortisol levels 30 minutes after documented hypoglycemia.
  - a. A rise in glucose secondary to glucagon  $\geq 30$  mg/dL along with elevated insulin levels, low serum levels of free fatty acids and  $\beta$ -hydroxybutyrate, and a glucose requirement  $>8$  mg/kg/min suggests a diagnosis of hyperinsulinemia.

- b. Hypoglycemia with midline defects and micropenis in a male suggest hypopituitarism, supported by low serum levels of growth hormone and cortisol at the time of hypoglycemia.

## IX. ADDITIONAL NORMAL VALUES

Please note that normal values may differ among laboratories because of variation in technique and type of assay used.

See Expert Consult, Chapter 10, for normal values of:

Table EC 10-A, Dihydrotestosterone (DHT)

Table EC 10-B, Catecholamines, urine

Table EC 10-C, Catecholamines, plasma

Table EC 10-D, Insulin-like growth factor binding protein

Table EC 10-E, Mean stretched penile length

Table EC 10-F, Androstenedione, serum

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TABLE EC 10-A

## DIHYDROTESTOSTERONE (DHT)

Age	Males (ng/dL)	Females (ng/dL)
Cord blood	<2–8	<2–5
1–6 mo	12–85	<5
Prepubertal	<5	<5
Tanner stage II–III	3–33	5–19
Tanner stage IV–V	22–75	3–30

Reference ranges from Quest Diagnostics RIA (radioimmunoassay).

TABLE EC 10-B

## CATECHOLAMINES, URINE

Compound	3–8 years	9–12 years	13–17 years	Adults
Dopamine (mcg/24 hr)	80–378	51–474	51–645	52–480
Epinephrine (mcg/24 hr)	1–7	≤8	≤11	2–14
Norepinephrine (mcg/24 hr)	5–41	5–50	12–88	15–100
Homovanillic acid (mg/24 hr)	0.5–6.7	1.1–6.8	1.4–7.2	1.6–7.5
Vanillyl mandelic acid (g/24 hr)	≤2.3	≤3.4	≤3.9	≤6.0

	3 mo–4 yr	5–9 years	10–13 years	14–17 years	18–29 years
Metanephrines (mcg/24 hr)	25–117	11–139	51–275	40–189	25–222
Normetanephrines (mcg/24 hr)	54–249	31–398	67–503	69–531	40–412

**NOTE:** Catecholamines are elevated in a variety of tumors, including neuroblastoma, ganglioneuroma, ganglioblastoma, and pheochromocytoma.

Reference ranges from JHH laboratories.

TABLE EC 10-C

## CATECHOLAMINES, PLASMA

	Supine (pg/mL)	Sitting (pg/mL)
<b>Epinephrine</b>		
3–15 yr	≤464	Not determined
Adult	≤50	≤95
<b>Norepinephrine</b>		
3–15 yr	≤1251	Not determined
Adult	112–658	217–1109
<b>Dopamine</b>		
3–15 yr	≤60	Not determined
Adult	≤30	≤30

From Blondell R, Foster MB, Dave KC. Disorders of puberty. *Am Family Phys.* 1999;60:209–218.

Reference ranges from JHH Laboratories.

**TABLE EC 10-D**  
**INSULIN-LIKE GROWTH FACTOR-BINDING PROTEIN (IGF-BP3)**

Age	mg/L	Tanner Stage	Female mg/L	Male mg/L
0–7 days	≤0.7	Tanner I	1.2–6.4	1.4–5.2
8–15 days	0.5–1.4	Tanner II	2.8–6.9	2.3–6.3
16 days–1 yr	0.7–3.6	Tanner III	3.9–9.4	3.2–8.9
2 yr	0.8–3.9	Tanner IV	3.3–8.1	3.7–8.7
3 yr	0.9–4.3	Tanner V	2.7–9.1	2.6–8.6
4 yr	1.0–4.7			
5 yr	1.1–5.2			
6 yr	1.3–5.6			
7 yr	1.4–6.1			
8 yr	1.6–6.5			
9 yr	1.8–7.1			
10 yr	2.1–7.7			
11 yr	2.4–8.4			
12 yr	2.7–8.9			
13 yr	3.1–9.5			
14 yr	3.3–10.0			
15 yr	3.5–10.0			
16 yr	3.4–9.5			
17 yr	3.2–8.7			
18 yr	3.1–7.9			
19 yr	2.9–7.3			

Adults continue to  
vary by age

**NOTE:** Levels below 5th percentile suggest growth hormone deficiency. This test may have greater discrimination than the IGF-1 test in younger patients.

Reference values from Quest Diagnostics immunochemiluminometric assay (ICMA).

TABLE EC 10-E

## MEAN STRETCHED PENILE LENGTH (CM)

Age	Mean $\pm$ SD	-2.5 SD
Birth		
30 wk gestation	2.5 $\pm$ 0.4	1.5
34 wk gestation	3.0 $\pm$ 0.4	2.0
Full term	3.5 $\pm$ 0.4	2.5
0-5 mo	3.9 $\pm$ 0.8	1.9
6-12 mo	4.3 $\pm$ 0.8	2.3
1-2 yr	4.7 $\pm$ 0.8	2.6
2-3 yr	5.1 $\pm$ 0.9	2.9
3-4 yr	5.5 $\pm$ 0.9	3.3
4-5 yr	5.7 $\pm$ 0.9	3.5
5-6 yr	6.0 $\pm$ 0.9	3.8
6-7 yr	6.1 $\pm$ 0.9	3.9
7-8 yr	6.2 $\pm$ 1.0	3.7
8-9 yr	6.3 $\pm$ 1.0	3.8
9-10 yr	6.3 $\pm$ 1.0	3.8
10-11 yr	6.4 $\pm$ 1.1	3.7
Adult	13.3 $\pm$ 1.6	9.3

**NOTE:** Measured from the pubic ramus to the tip of the glans while traction is applied along the length of the phallus to the point of increased resistance.

SD, Standard deviation.

From Feldman KW, Smith DW. Fetal phallic growth and penile standards for newborn male infants. *J Pediatr*. 1975;86:395.

TABLE EC 10-F

## ANDROSTENEDIONE, SERUM

Age	Males (ng/dL)	Females (ng/dL)
Premature (31-35 wk)	$\leq 480$	$\leq 480$
Full-term infants	$\leq 290$	$\leq 290$
1-12 mo	6-78	6-78
1-4 yr	5-51	5-51
5-9 yr	6-115	6-115
10-13 yr	12-221	12-221
14-17 yr	22-225	22-225
Tanner stage II-III	17-82	43-180
Tanner stage IV-V	57-150	73-220
Adult male (18-30 yr)	50-220	
Female follicular phase		35-250
Female luteal phase		30-235

Values from Quest Diagnostics LC/MS (liquid chromatography/tandem mass spectrometry) analysis.

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# Chapter 11

## Fluids and Electrolytes

Emily Young Thomas, MD

 See additional content on Expert Consult

### I. OVERALL GUIDANCE IN FLUID AND ELECTROLYTE MANAGEMENT

#### A. Goals

Fluid therapy is an essential component of the care of hospitalized children. The basic principles should be followed whether providing oral or parenteral fluids. Appropriate fluid management involves the calculation and administration of water volume and electrolyte concentration of:

1. **Maintenance requirements**
2. **Initial deficit repletion**
3. **Ongoing losses**

#### B. The purpose of this chapter is to help one understand:

1. **Proper water and electrolyte needs to maintain homeostasis** - see [Section II.A](#). Although calculations demonstrate that  $\frac{1}{4}$  normal saline (0.225% NaCl) supplies maintenance solute needs, the majority of acutely ill pediatric patients have solute needs beyond maintenance requirements (see [Section II.B.2](#)).
2. **Potential complications of using  $\frac{1}{4}$  normal saline (NS) in an acutely ill patient.** An increased number of case studies have reported complications from using  $\frac{1}{4}$  NS for acutely ill patients, most notably hospital-acquired hyponatremia.<sup>1-4</sup>
3. **How the clinical context of an individual patient, rather than dogma, should dictate the proper fluid therapy for a child.**
  - a. For example, a child who is being hospitalized before surgery and is otherwise well only requires maintenance fluids;  $\frac{1}{4}$  NS may be an appropriate choice.
  - b. Postoperatively, however, this same child will likely have developed deficits or conditions that increase the release of antidiuretic hormone (ADH), so one should strongly reconsider using  $\frac{1}{4}$  NS in this patient. For more conditions that increase ADH release, please see [Box EC 11-A](#).<sup>1</sup>

### II. MAINTENANCE REQUIREMENTS

Maintenance requirements are the amount of water and electrolytes lost during normal basal metabolism. Metabolism creates two byproducts, heat and solute, that must be eliminated to maintain homeostasis. The amount of heat dissipated through insensible water losses and the amount of solute excreted in urine are directly related to caloric expenditure.

## BOX EC 11-A

## CLINICAL SETTING OF INCREASED ADH RELEASE IN CHILDREN

**Hemodynamic Stimuli for ADH Release  
(Decreased Effective Volume)**

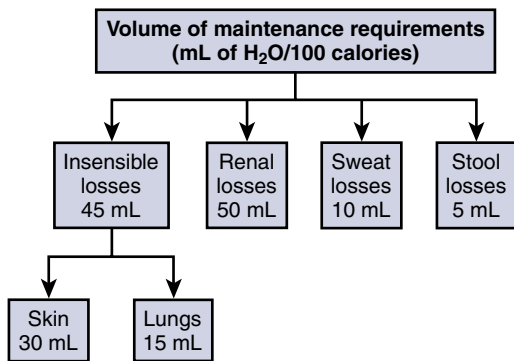
Hypovolemia  
Nephrosis  
Cirrhosis  
Congestive heart failure  
Hypoaldosteronism  
Hypotension  
Hypoalbuminemia

**Nonhemodynamic Stimuli for  
ADH Release**

CNS disturbances (meningitis,  
encephalitis, brain tumors, head  
injury)  
Pulmonary disease (pneumonia,  
asthma, bronchiolitis)  
Cancer  
Medications (cytoxan, vincristine,  
morphine)  
GI disturbances (nausea, emesis)  
Pain or stress  
Postoperative state

ADH, Antidiuretic hormone; CNS, central nervous system; GI, gastrointestinal.

Modified from Moritz ML, Ayus JC. Prevention of hospital-acquired hyponatremia: a case for using isotonic saline. *Pediatrics*. 2003;111:227-230.

**FIGURE 11-1**

For each 100 calories metabolized in 24 hours, about 55–60 mL of fluid is required to provide for insensible losses as well as basal stool and sweat losses, and 50 mL of fluid is required for the kidneys to excrete an ultrafiltrate of plasma at 300 mOsm/L without having to concentrate the urine. (Modified from Roberts KB. *Fluids and electrolytes: parenteral fluid therapy*. *Pediatr Rev*. 2001;22:380-387.)

Metabolic demands do not increase in direct proportion to body mass (weight) across the continuum. The metabolic rate per kg body weight declines with age; an infant generates significantly more solute and heat per kg than a child or adolescent. To correctly calculate maintenance needs, it is necessary to determine calories burned (Fig. 11-1).<sup>5</sup>

### A. Maintenance Volume: Caloric Calculations

There are three basic methods to calculate maintenance fluid volume needs:

1. **Basal calorie method:** Useful for all ages, types of body habitus, and clinical states
  - a. Determine the child's estimated energy requirements based on age and activity level (see Table 21-2).
  - b. Adjust caloric expenditure needs by various factors as described in Chapter 21.
  - c. For each 100 calories metabolized in 24 hours, the average patient will need 100–120 mL H<sub>2</sub>O, 2–4 mEq Na<sup>+</sup>, and 2–3 mEq K<sup>+</sup>.
2. **Holliday-Segar method** (Table 11-1 and Box 11-1)<sup>6</sup>: Estimates caloric expenditure in fixed-weight categories and makes the same assumption for water and electrolyte needs based on 100 kcal burned as above (refer to A.1.c of this section)

**NOTE:** The Holliday-Segar method is not suitable for neonates <14 days old; generally it overestimates fluid needs in neonates compared with the caloric expenditure method. (See Chapter 18 for further neonatal fluid management.)

**TABLE 11-1**  
**HOLLIDAY-SEGAR METHOD**

Body Weight	Water	
	mL/kg/day	mL/kg/hr
First 10 kg	100	≈4
Second 10 kg	50	≈2
Each additional kg	20	≈1

To calculate needed electrolytes:  $\text{Na}^+$  3 mEq/100 mL  $\text{H}_2\text{O}$ ;  $\text{Cl}^-$  2 mEq/100 mL  $\text{H}_2\text{O}$ ;  $\text{K}^+$  2 mEq/100 mL  $\text{H}_2\text{O}$ .

**BOX 11-1**  
**HOLLIDAY-SEGAR METHOD**

Example: Determine the correct fluid rate for an 8-year-old child weighing 25 kg:

First 10 kg:	$4 \text{ mL/kg/hr} \times 10 \text{ kg} =$ 40 mL/hr	$100 \text{ mL/kg/day} \times 10 \text{ kg} =$ 1000 mL/day
Second 10 kg:	$2 \text{ mL/kg/hr} \times 10 \text{ kg} =$ 20 mL/hr	$50 \text{ mL/kg/day} \times 10 \text{ kg} =$ 500 mL/day
Each additional 1 kg:	$1 \text{ mL/kg/hr} \times 5 \text{ kg} =$ 5 mL/hr	$20 \text{ mL/kg/day} \times 5 \text{ kg} =$ 100 mL/day
	Answer: 65 mL/hr	Answer: 1600 mL/day

**TABLE 11-2**  
**STANDARD VALUES FOR USE IN BODY SURFACE AREA (BSA) METHOD**

$\text{H}_2\text{O}$	1500 mL/m <sup>2</sup> /24 hr
$\text{Na}^+$	30–50 mEq/m <sup>2</sup> /24 hr
$\text{K}^+$	20–40 mEq/m <sup>2</sup> /24 hr

m<sup>2</sup> = meters squared.

3. **Body surface area (BSA) method:** Based on the assumption that caloric expenditure is related to body surface area (BSA) (Table 11-2).<sup>7,8</sup> It should not be used for children <10 kg. See BSA calculation in Formula Adjunct Figure 30-1.

**B. Maintenance Solute**

1. **For the purposes of fluid calculation,** fluid lost via insensible losses through the skin and respiratory tract can be considered electrolyte free. Urine represents the primary source of electrolyte loss, with variability based on the kidney's ability to dilute and concentrate. Average electrolyte requirements per 100 mL  $\text{H}_2\text{O}$  are seen in the legend of Table 11-1, with the addition of 5%–10% dextrose (depending on need) to prevent ketosis. Solute needs can thus be met by administering  $\text{D}_5\frac{1}{4}\text{NS}$  with 20 mEq/L KCl.
2. **Cautions regarding 1/4 NS fluid administration:** Many hospitalized patients have water and electrolyte deficits and may retain free water owing to various disease processes. Prior or ongoing losses of water or electrolytes require further volume and electrolyte deficit calculations

and appropriate adjustment of replacement fluids in their management (see Table 11-6).

### III. DEFICIT REPLETION

The following equations are numbered and can be used to calculate fluid management per Fig. 11-2, based on the amount of fluid/electrolytes lost before a patient's hospital presentation.

#### A. Water Deficit Volume

1. **Calculated assessment:** Most precise method of assessing fluid deficit is weight loss. If this is not known, clinical observation may be used:

$$\text{Water deficit (L)} = \text{pre-illness weight (kg)} - \text{illness weight (kg)} \quad (\text{Equation A.1})$$

$$\% \text{ Dehydration} = (\text{pre-illness weight} - \text{illness weight}) / \text{pre-illness weight} \times 100\%$$

2. **Clinical assessment** (Table 11-3)<sup>9,10</sup>: Each 1% dehydration corresponds to 10 mL/kg fluid deficit

#### B. Solute Deficit Based on Solute Fluid Deficit (Isonatremic Dehydration)

Fluid losses from intracellular and extracellular compartments are used to determine electrolyte deficit and replacement.

**NOTE:** These calculations hold true for isonatremic dehydration. To calculate solute deficit in hypernatremic dehydration, see Section E.

1. **Extracellular fluid compartment:**  $\approx 20\%$  of the body's weight (40% in the newborn), divided 3:1 between interstitial and intravascular compartments, respectively.<sup>11</sup>
2. **In dehydration**, there are variable losses from the extracellular and intracellular compartments. The percentage deficit from these compartments is based on the total duration of illness.
  - a. Illness  $< 3$  days: 80% (0.8) extracellular fluid (ECF) deficit, 20% (0.2) intracellular fluid (ICF) deficit
  - b. Illness  $\geq 3$  days: 60% (0.6) ECF deficit, 40% (0.4) ICF deficit
3. **Composition of intracellular and extracellular fluid:** Shown in Table 11-4.
4. **Na<sup>+</sup> deficit:** Amount of Na<sup>+</sup> lost from the Na<sup>+</sup>-containing ECF compartment during the dehydration period. Intracellular Na<sup>+</sup> is negligible as a proportion of total and can be disregarded (see Table 11-4).

$$\text{Na}^+ \text{ deficit (mEq)} = \text{fluid deficit (L)} \times \text{proportion from ECF} \times \text{Na}^+ \text{ concentration (mEq/L) in ECF} \quad (\text{Equation F.1})$$

*A 25-kg (pre-illness weight) child who has been ill  $> 3$  days is 9% dehydrated, with serum [Na<sup>+</sup>] 137 mEq/L:*

$$\text{Fluid deficit} = (90 \text{ mL/kg}) (25 \text{ kg}) = 2250 \text{ mL}$$

$$\text{Na}^+ \text{ deficit} = (2.25 \text{ L}) (0.6) (137 \text{ mEq/L}) = 184 \text{ mEq}$$

Isonatremic Dehydration			
	EQ	First 8 hours	Next 16 hours
Fluid deficit volume	A.1	Replace ½ of calculated deficits divided evenly over 8 hours.	Replace remaining ½ of calculated deficits divided evenly over 16 hours.
Na <sup>+</sup> deficit	F.1		
K <sup>+</sup> deficit	F.2		
Maintenance		To be given in addition to above calculated deficits at hourly rate.	

Hyponatremic Dehydration			
	EQ	First 8 hours	Next 16 hours
Fluid deficit volume	A.1	Replace ½ of calculated deficits divided evenly over 8 hours.	Replace remaining ½ of calculated deficits divided evenly over 16 hours.
Na <sup>+</sup> deficit	F.1		
Excess Na <sup>+</sup> deficit	F.3		
K <sup>+</sup> deficit	F.2		
Maintenance		To be given in addition to above calculated deficits at hourly rate.	

Hypernatremic Dehydration				
	EQ	First 8 hours	Next 16 hours	Next 24 hours
Free water deficit	F.4	Replace ½ of deficit over first 24 hours.		Replace remaining ½ of calculated deficit over next 24 hours.
Solute fluid deficit	F.5	Replace ½ of calculated deficits divided evenly over 8 hours.	Replace remaining ½ of calculated deficits divided evenly over 16 hours.	
Solute Na <sup>+</sup> deficit	F.6			
Solute K deficit	F.7			
Maintenance		To be given in addition to above calculated deficits at hourly rate.		

FIGURE 11-2

Fluid and solute replacement in isonatremic, hyponatremic, and hypernatremic dehydration.

TABLE 11-3

## CLINICAL OBSERVATIONS IN DEHYDRATION\*

	Older Child		
	3% (30 mL/kg)	6% (60 mL/kg)	9% (90 mL/kg)
	Infant		
	5% (50 mL/kg)	10% (100 mL/kg)	15% (150 mL/kg)
<b>EXAMINATION</b>			
Dehydration	Mild	Moderate	Severe
Skin turgor	Normal	Tenting	None
Skin (touch)	Normal	Dry	Clammy
Buccal mucosa/lips	Dry	Dry	Parched/cracked
Eyes	Normal	Deep set	Sunken
Tears	Present	Reduced	None
Fontanelle	Flat	Soft	Sunken
Mental status	Alert		Lethargic/obtunded
Pulse rate	Normal	Slightly increased	Increased
Pulse quality	Normal	Weak	Feeble/impalpable
Capillary refill	Normal	≈2-3 seconds	>3 seconds
Urine output	Normal/mild oliguria	Mild oliguria	Severe oliguria

\*Serum sodium concentration affects the clinical manifestations of dehydration, such as skin turgor and mucous membranes. For example, hyponatremia exaggerates instability, and hypernatremia maintains intravascular volume at the expense of intracellular volume.

TABLE 11-4

## INTRACELLULAR AND EXTRACELLULAR FLUID COMPOSITION

	Intracellular (mEq/L)	Extracellular (mEq/L)
Na <sup>+</sup>	20	133–145
K <sup>+</sup>	150	3–5
Cl <sup>−</sup>	—	98–110
HCO <sub>3</sub> <sup>−</sup>	10	20–25
PO <sub>4</sub> <sup>3−</sup>	110–115	5
Protein	75	10
% Body weight	80	15 (interstitial), 5 (intravascular)

5. **K<sup>+</sup> deficit:** Amount of K<sup>+</sup> lost from the K<sup>+</sup>-containing ICF compartment during the dehydration period. Extracellular K<sup>+</sup> is negligible as a proportion of total and can be disregarded (see Table 11-4).

$$\text{K}^+ \text{ deficit (mEq)} = \text{fluid deficit (L)} \times \text{proportion from ICF} \times \text{K}^+ \text{ concentration (mEq/L) in ICF} \quad (\text{Equation F.2})$$

*A 25-kg (pre-illness weight) child who has been ill >3 days and is 9% dehydrated:*

$$\text{K}^+ \text{ deficit} = (2.25 \text{ L}) (0.4) (150 \text{ mEq/L}) = 135 \text{ mEq}$$



### C. Excess Electrolyte Deficits

The amount of additional  $\text{Na}^+$  or  $\text{K}^+$  deficit calculated based on serum laboratory findings. Typically calculated in hyponatremic dehydration.

$$\text{mEq required} = [\text{concentration desired (mEq/L)} - \text{concentration present (mEq/L)}] \times \text{fD} \times \text{weight (kg, pre-illness)} \quad (\text{Equation F.3})$$

fD = distribution factor as fraction of body weight (L/kg):  $\text{HCO}_3^-$  (0.4 – 0.5);  $\text{Cl}^-$  (0.2 – 0.3);  $\text{Na}^+$  (0.6 – 0.7)

*A 25-kg (pre-illness weight) child who has been ill >3 days and is 9% dehydrated, with serum  $[\text{Na}^+]$  117 mEq/L:*

$$\text{Excess } \text{Na}^+ \text{ deficit} = (135 \text{ mEq/L} - 117 \text{ mEq/L}) (0.6) (25 \text{ kg}) = 270 \text{ mEq}$$

### D. Free Water Deficit (FWD)

The amount of additional free water loss in a patient with **hypernatremic dehydration**. Based on estimates that it requires 4 mL/kg to decrease serum  $\text{Na}^+$  by 1 mEq/L. **NOTE:** If serum  $\text{Na}^+$  is >170, estimate decreases to 3 mL/kg.

$$\text{FWD (mL)} = 4 \text{ mL/kg} \times \text{pre-illness weight (kg)} \times [\text{concentration present (mEq/L)} - \text{concentration desired (mEq/L)}] \quad (\text{Equation F.4})$$

*A 25-kg (pre-illness weight) child who has been ill >3 days and is 9% dehydrated, with serum  $[\text{Na}^+]$  160 mEq/L:*

$$\text{FWD} = (4 \text{ mL/kg}) (25 \text{ kg}) (160 \text{ mEq/L} - 145 \text{ mEq/L}) = 1500 \text{ mL}$$

### E. Solute Fluid Deficit (SFD)

The amount of additional fluid volume loss beyond free water loss in a patient with **hypernatremic dehydration**. The SFD is subsequently used to calculate  $\text{Na}^+$  and  $\text{K}^+$  deficits in these patients.

$$\text{SFD} = \text{total fluid deficit} - \text{FWD} \quad (\text{Equation F.5})$$

*A 25-kg (pre-illness weight) child who has been ill >3 days and is 9% dehydrated, with serum  $[\text{Na}^+]$  160 mEq/L:*

$$\text{Total fluid deficit} = (90 \text{ mL/kg}) (25 \text{ kg}) = 2250 \text{ mL}$$

$$\text{SFD} = 2250 \text{ mL} - 1500 \text{ mL} = 750 \text{ mL}$$

$$\text{Solute } \text{Na}^+ \text{ deficit (mEq/L)} = \text{SFD (L)} \times \text{proportion from ECF} \times \text{Na}^+ \text{ concentration (mEq/L) in ECF} \quad (\text{Equation F.6})$$

$$\text{Solute } \text{Na}^+ \text{ deficit} = (0.75 \text{ L}) (0.6) (145 \text{ mEq/L}) = 65 \text{ mEq}$$

$$\text{Solute K}^+ \text{ deficit (mEq/L)} = \text{SFD (L)} \times \text{proportion from ICF} \times \text{K}^+ \text{ concentration (mEq/L) in ICF} \quad (\text{Equation F.7})$$

$$\text{Solute K}^+ \text{ deficit} = (0.75 \text{ L}) (0.4) (150 \text{ mEq/L}) = 45 \text{ mEq}$$

## F. Deficit Replacement Strategy

1. **Phase I:** Rapid fluid resuscitation with isotonic fluid (NS or lactated Ringers [LR])
  - a. Should be reserved for patients with need for rapid volume expansion (see Chapter 1). Generally, administration of isotonic fluid expands intravascular volume without causing significant fluid shifts, but overadministration of isotonic fluids can be dangerous in patients with hyperosmolality (e.g., diabetic ketoacidosis [DKA] with hyperglycemia).
  - b. Recognize that a bolus of 20 mL/kg represents only a 2% body weight replacement. A child calculated to be above 2% dehydrated will not be sufficiently repleted after an initial single bolus.
  - c. Consider subtracting fluid and electrolytes given during resuscitation from the total deficits when calculating replacement of fluid and electrolytes.
2. **Phase II:** Deficit repletion, maintenance, and ongoing losses  
After initial stabilization, the remaining deficit is replaced over the next 24–48 hours. Replace half of the remaining deficit over the first 8 hours and the second half over the following 16 hours (with the exception of free water deficit, which is replaced over 48 hours), in addition to the previously calculated maintenance fluid rate. See [Fig. 11-2](#) for calculation of fluid and solute replacement in isonatremic, hyponatremic, and hypernatremic dehydration.
  - a. **Hyponatremic dehydration:** Excess  $\text{Na}^+$  loss ( $\text{Na}^+ < 130 \text{ mEq/L}$ ). Rapid correction of serum  $\text{Na}^+$  could result in central pontine myelinolysis and should be reserved for symptomatic patients. In asymptomatic patients, the rate of rise should not exceed 0.5–1 mEq/L per hour, or 10–12 mEq/L in 24 hours.
  - b. **Isonatremic dehydration:** Proportional losses of Na and free water ( $\text{Na}^+ 130\text{--}149 \text{ mEq/L}$ ).
  - c. **Hypernatremic dehydration:** Excess free water loss ( $\text{Na}^+ > 150 \text{ mEq/L}$ ). Avoid dropping the serum  $\text{Na}^+$  by  $>15 \text{ mEq/L}$  per 24 hours to minimize the risk of cerebral edema.
  - d. See [Tables EC 11-A, 11-B, and 11-C](#) for sample calculations of fluid and solute replacement in isonatremic, hyponatremic, and hypernatremic dehydration.

## G. Calculation of Appropriate Fluids

After completing the previous calculations for the patient, divide the desired amount of each solute by the total volume of fluid required to calculate the concentration of fluid and additives. Choose the appropriate corresponding fluid from [Table 11-5](#), and add any other necessary solute components.

TABLE EC 11-A

## EXAMPLE OF ISONATREMIC DEHYDRATION

Deficit Replacement	H <sub>2</sub> O (mL)	Na <sup>+</sup> (mEq)	K <sup>+</sup> (mEq)
Determine an adequate fluid schedule for a 7-kg (pre-illness weight) infant who has been ill for ≥3 days and clinically appears 10% dehydrated. Current weight is 6.3 kg. Serum Na <sup>+</sup> = 137 mEq/L. An intravenous (IV) line has just been placed, but no IV fluid has been administered.			

## FLUID DEFICIT

$$\% \text{ Dehydration} \times \text{wt (kg)} = 10\% \times 7 \text{ kg} \times 700 \text{ (1000 mL/kg)}$$

Na<sup>+</sup> Deficit

$$0.7 \times 0.6 \times 145 = 61$$

K<sup>+</sup> Deficit

$$0.7 \times 0.4 \times 150 = 21$$

## MAINTENANCE

H<sub>2</sub>O

$$7 \text{ kg} \times 100 \text{ mL/kg/day} = 700$$

Na<sup>+</sup>

$$700 \text{ mL/day} \times 3 \text{ mEq/100 mL} = 21$$

K<sup>+</sup>

$$700 \text{ mL/day} \times 2 \text{ mEq/100 mL} = 14$$

<b>24-HR TOTAL</b>	<b>1400</b>	<b>82</b>	<b>56</b>
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## Fluid Schedule

## First 8 hr

$\frac{1}{3}$ maintenance	233	7	5
---------------------------	-----	---	---

$\frac{1}{2}$ deficit	350	31	21
-----------------------	-----	----	----

First 8-hr total	583	38	26
------------------	-----	----	----

## Next 16 hr

$\frac{2}{3}$ maintenance	467	14	9
---------------------------	-----	----	---

$\frac{1}{2}$ deficit	350	30	21
-----------------------	-----	----	----

Next 16-hr total	817	44	30
------------------	-----	----	----

## ANSWER

Therefore, first 8 hr:

$$\text{Rate: } 583 \text{ mL/8 hr} = 73 \text{ mL/hr}$$

$$\text{Na}^+: 38 \text{ mEq}/0.583 \text{ L} = 65 \text{ mEq/L}$$

$$\text{K}^+: 26 \text{ mEq}/0.583 \text{ L} = 45 \text{ mEq/L}$$

$$\text{D}_5 \frac{1}{2} \text{ NS} + 40 \text{ mEq/L of KCl or K acetate} \\ @ \approx 75 \text{ mL/hr} \times 8 \text{ hr}$$

Next 16 hr:

$$\text{Rate: } 817 \text{ mL}/16 \text{ hr} = 51 \text{ mL/hr}$$

$$\text{Na}^+: 44 \text{ mEq}/0.817 \text{ L} = 54 \text{ mEq/L}$$

$$\text{K}^+: 30 \text{ mEq}/0.817 \text{ L} = 37 \text{ mEq/L}$$

$$\text{D}_5 \frac{1}{2} \text{ NS} + 40 \text{ mEq/L of KCl or K acetate} \\ @ \approx 50 \text{ mL/hr} \times 16 \text{ hr}$$

In the absence of hypokalemia, 20–30 mEq/L of potassium is commonly used and typically adequate. Monitor carefully for hyperkalemia and adequate urine output if high concentrations of potassium are used. Potassium infusion rates should not exceed 1 mEq/kg/hr. If rate exceeds 0.5 mEq/kg/hr, the patient should be placed on a cardiorespiratory monitor.

**NOTE:** Remember to account for ongoing losses. They should be replaced concurrently (piggybacked) with a solution that matches the fluid being lost (see Table 11-6).

TABLE EC 11-B

## EXAMPLE OF HYPONATREMIC DEHYDRATION

Deficit Replacement	H <sub>2</sub> O (mL)	Na <sup>+</sup> (mEq)	K <sup>+</sup> (mEq)
Determine an adequate fluid schedule for a 7-kg (pre-illness weight) infant who has been ill for ≥3 days and clinically appears 10% dehydrated. Current weight is 6.3 kg. Serum Na <sup>+</sup> = 115 mEq/L. An intravenous (IV) line has just been placed, but no IV fluid has been administered.			
<b>FLUID DEFICIT</b>			
% Dehydration × wt (kg) = 10% × 7 kg × (1000 mL/kg)	700		
<b>Na<sup>+</sup> Deficit</b>			
0.7 × 0.6 × 145 =		61	
Excess Na <sup>+</sup> deficit: (135–115) × 0.6 × 7 =		84	
<b>K<sup>+</sup> Deficit</b>			
0.7 × 0.4 × 150 =			42
<b>MAINTENANCE</b> (See Table EC 11-A)	700	21	14
<b>24-HR TOTAL</b>	1400	166	56
<b>Fluid Schedule</b>			
First 8 hr			
1/3 maintenance	233	7	5
1/2 deficit	350	73	21
First 8-hr total	583	80	26
Next 16 hr			
2/3 maintenance	467	14	9
1/2 deficit	350	72	21
Next 16-hr total	817	86	30
<b>ANSWER</b>			
Therefore, first 8 hr:	Next 16 hr:		
Rate: 583 mL/8 hr = 73 mL/hr	Rate: 817 mL/16 hr = 51 mL/hr		
Na <sup>+</sup> : 80 mEq/0.583 L = 137 mEq/L	Na <sup>+</sup> : 86 mEq/0.817 L = 105 mEq/L		
K <sup>+</sup> : 26 mEq/0.583 L = 45 mEq/L	K <sup>+</sup> : 30 mEq/0.817 L = 37 mEq/L		
<b>D<sub>5</sub>NS + 40 mEq/L of KCl or K acetate</b>	<b>D<sub>5</sub> 1/2 NS + 40 mEq/L of KCl or K acetate</b>		
@ ≈ 75 mL/hr × 8 hr	@ ≈ 50 mL/hr × 16 hr		

In the absence of hypokalemia, 20–30 mEq/L of potassium is commonly used and typically adequate. Monitor carefully for hyperkalemia and adequate urine output if high concentrations of potassium are used. Potassium infusion rates should not exceed 1 mEq/kg/hr. If rate exceeds 0.5 mEq/kg/hr, the patient should be placed on a cardiorespiratory monitor.

**NOTE:** Remember to account for ongoing losses. They should be replaced concurrently (piggybacked) with a solution that matches the fluid being lost (see Table 11-6).

TABLE EC 11-C

## EXAMPLE OF HYPERNATREMIC DEHYDRATION

Replacement	H <sub>2</sub> O (mL)	Na <sup>+</sup> (mEq)	K <sup>+</sup> (mEq)
Determine an adequate fluid schedule for a 7-kg (pre-illness weight) infant who has been ill for ≥3 days and clinically appears between 10% and 15% dehydrated. Current weight is 6.1 kg. Serum Na <sup>+</sup> = 160 mEq/L.			
<b>FREEWATER DEFICIT (FWD)</b>			
$4 \text{ mL/kg} \times 7 \text{ kg} \times [160-145] =$	420		
<b>SOLUTE FLUID DEFICIT (SFD)</b>			
$[ \text{Total fluid deficit (900)} ] - [\text{FWD}]$	480		
<b>SOLUTE Na<sup>+</sup> DEFICIT</b>			
$0.48 \times 0.6 \times 145 =$		42	
<b>SOLUTE K<sup>+</sup> DEFICIT</b>			
$0.48 \times 0.4 \times 150 =$			29
<b>MAINTENANCE</b> (see Table EC 11-A)	700	21	14
<b>FLUID SCHEDULE</b>			
First 24 hr			
24-hr maintenance	700	21	14
½ FWD	210		
Solute fluid and electrolyte deficit	480	42	29
First 24-hr total	1390	63	43
Second 24 hr			
Second 24-hr maintenance	700	21	14
½ FWD	210		
Second 24-hr total	910	21	14
<b>ANSWER</b>			
Therefore, first 24 hr:	Second 24 hr:		
Rate: $1390 \text{ mL}/24 \text{ hr} = 58 \text{ mL/hr}$	Rate: $910 \text{ mL}/24 \text{ hr} = 38 \text{ mL/hr}$		
Na <sup>+</sup> : $63 \text{ mEq}/1.39 \text{ L} = 45 \text{ mEq/L}$	Na <sup>+</sup> : $21 \text{ mEq}/0.91 \text{ L} = 23 \text{ mEq/L}$		
K <sup>+</sup> : $43 \text{ mEq}/1.39 \text{ L} = 31 \text{ mEq/L}$	K <sup>+</sup> : $14 \text{ mEq}/0.91 \text{ L} = 15 \text{ mEq/L}$		
<b>D<sub>5</sub> NS + 30 mEq/L KCl or K acetate</b>	<b>D<sub>5</sub> NS + 10 mEq/L KCl or K acetate</b>		
<b>@ 58 mL/hr × 24 hr</b>	<b>@ 38 mL/hr × 24 hr</b>		

Follow serum Na<sup>+</sup>, and adjust fluid composition and rate based on clinical response. The second half of the FWD may be replaced subsequently over the next 24 hr, or more rapidly depending on the rate of decline of serum Na<sup>+</sup> (avoid decline of >15 mEq/L in 24 hr).

**NOTE:** In severe hypernatremic dehydration, initial lactated Ringer's/normal saline solution resuscitation boluses should be accounted for to minimize dropping serum sodium >15 mEq/L per 24 hr to minimize risk of cerebral edema.

TABLE 11-5

## COMPOSITION OF FREQUENTLY USED PARENTERAL AND ORAL REHYDRATION FLUIDS

	D% CHO (g/100 mL)	Protein* (g/100 mL)	Cal/L	Na <sup>+</sup> (mEq/L)	K <sup>+</sup> (mEq/L)	Cl <sup>-</sup> (mEq/L)	HCO <sub>3</sub> <sup>-†</sup> (mEq/L)	Ca <sup>2+</sup> (mEq/L)	mOsm/L
<b>PARENTERAL FLUID</b>									
D <sub>5</sub> W	5	—	170	—	—	—	—	—	252
D <sub>10</sub> W	10	—	340	—	—	—	—	—	505
NS (0.9% NaCl)	—	—	—	154	—	154	—	—	308
½ NS (0.45% NaCl)	—	—	—	77	—	77	—	—	154
D <sub>5</sub> ¼ NS (0.225% NaCl)	5	—	170	34	—	34	—	—	329
3% NaCl	—	—	—	513	—	513	—	—	1027
8.4% sodium bicarbonate (1 mEq/mL)	—	—	—	1000	—	—	1000	—	2000
Ringer's solution	0–10	—	0–340	147	4	155.5	—	≈4	—
Lactated Ringer's	0–10	—	0–340	130	4	109	28	3	273
Amino acid 8.5% (Travasol)	—	8.5	340	3	—	34	52	—	880
Plasmanate	—	5	200	110	2	50	29	—	—
Albumin 25% (salt poor)	—	25	1000	100–160	—	<120	—	—	300
Intralipid <sup>‡</sup>	2.25	—	1100	2.5	0.5	4.0	—	—	258–284
<b>ORAL FLUID</b>									
Pedialyte	2.5	—	—	45	20	35	30	—	250
WHO Solution	2	—	—	90	20	80	30	—	310
Rehydralyte	2.5	—	—	75	20	65	30	—	310

TABLE 11-5

## COMPOSITION OF FREQUENTLY USED PARENTERAL AND ORAL REHYDRATION FLUIDS (Continued)

	D% CHO (g/100 mL)	Protein* (g/100 mL)	Cal/L	Na <sup>+</sup> (mEq/L)	K <sup>+</sup> (mEq/L)	Cl <sup>-</sup> (mEq/L)	HCO <sub>3</sub> <sup>-†</sup> (mEq/L)	Ca <sup>2+</sup> (mEq/L)	mOsm/L
APPROXIMATE ELECTROLYTE COMPOSITION OF COMMONLY CONSUMED FLUIDS (NOT RECOMMENDED FOR ORAL REHYDRATION THERAPY)**									
Apple juice	11.9	—	—	0.4	26	—	—	—	700
Coca-Cola	10.9	—	—	4.3	0.1	—	13.4	—	656
Gatorade	5.9	—	—	21	2.5	17	—	—	377
G2	4.7	—	—	20	3.2	—	—	—	—
Ginger ale	9	—	—	3.5	0.1	—	3.6	—	565
Milk	4.9	—	—	22	36	28	30	—	260
Orange juice	10.4	—	—	0.2	49	—	50	—	654
Powerade	5.8	—	—	18	2.7	—	—	—	264

\*Protein or amino acid equivalent.

†Bicarbonate or equivalent (citrate, acetate, lactate).

‡Values are approximate; may vary from lot to lot. Also contains &lt;1.2% egg-phosphatides.

\*\*Values vary slightly depending on source.

CHO, Carbohydrate; HCO<sub>3</sub><sup>-</sup>, bicarbonate; NS, normal saline; WHO, World Health Organization.

**TABLE 11-6**

**ELECTROLYTE COMPOSITION OF VARIOUS BODY FLUIDS**

Fluid	Na <sup>+</sup> (mEq/L)	K <sup>+</sup> (mEq/L)	Cl <sup>-</sup> (mEq/L)	Replacement Fluid
Gastric	20–80	5–20	100–150	½ NS
Pancreatic	120–140	5–15	90–120	NS
Small bowel	100–140	5–15	90–130	NS
Bile	120–140	5–15	80–120	NS
Ileostomy	45–135	3–15	20–115	1/2 NS or NS
Diarrhea	10–90	10–80	10–110	½ NS
Burns*	140	5	110	NS or LR
Sweat				
Normal	10–30	3–10	10–35	1/2 NS
Cystic fibrosis†	50–130	5–25	50–110	

\*3–5 g/dL of protein may be lost in fluid from burn wounds.

†Replacement fluid dependent on sodium content.

LR, Lactated Ringer's; NS, normal saline.

1. **Parenteral fluid composition** (Table 11-5)

2. **Oral fluid composition** (Table 11-5)

Oral rehydration therapy should be used in patients with mild to moderate dehydration without signs of shock, coma, acute abdomen, gastric distension, intractable vomiting, or excess stool losses

- a. Method: Give 5–10 mL of oral rehydration solution (ORS) every 5–10 minutes, gradually increasing volume.
- b. Deficit replacement:
  - (1) Mild dehydration = 50 mL/kg over 4 hours
  - (2) Moderate dehydration = 100 mL/kg over 4 hours
- c. Maintenance: Infants should resume formula/breast milk by mouth (PO) ad lib. Children should continue with regular diet.
- d. Ongoing losses: Regardless of the degree of dehydration, give additional 10 mL/kg of ORS for each additional diarrheal stool.

**IV. ONGOING LOSSES**

Represent continued losses of fluid and solute after initial presentation, as in persistent vomiting and/or diarrhea, high fever with diuresis, or nasogastric suction. Some of these losses can be measured directly and appropriately replaced based on known electrolyte concentrations (Table 11-6).<sup>9</sup>

**V. SERUM ELECTROLYTE DISTURBANCES**

**A. Sodium**

1. **Hyponatremia:**

- a. Etiologies, diagnostic studies, and management (Table 11-7)
- b. Factitious etiologies:
  - (1) Hyperlipidemia: Na<sup>+</sup> decreased by 0.002 × lipid (mg/dL)
  - (2) Hyperproteinemia: Na<sup>+</sup> decreased by 0.25 × [protein (g/dL) – 8]



TABLE 11-7

## HYPONATREMIA\*

Decreased Weight		
Renal Losses	Extrarenal Losses	Increased or Normal Weight
Na <sup>+</sup> -losing nephropathy	GI losses	Nephrotic syndrome
Diuretics	Skin losses	Congestive heart failure
Adrenal insufficiency	Third spacing	SIADH (see Chapter 10)
Cerebral salt-wasting syndrome	Cystic fibrosis	Acute/chronic renal failure
		Water intoxications
		Cirrhosis
		Excess salt-free infusions
LABORATORY DATA		
↑ Urine Na <sup>+</sup>	↓ Urine Na <sup>+</sup>	↓ Urine Na <sup>+</sup> †
↑ Urine volume	↓ Urine volume	↓ Urine volume
↓ Specific gravity	↑ Specific gravity	↑ Specific gravity
↓ Urine osmolality	↑ Urine osmolality	↑ Urine osmolality
MANAGEMENT (IN ADDITION TO TREATING UNDERLYING CAUSE)		
Replace losses	Replace losses	Restrict fluids

\*Hyperglycemia and hyperlipidemia cause spurious hyponatremia.

†Urine Na<sup>+</sup> may be appropriate for level of Na<sup>+</sup> intake in patients with SIADH and water intoxication.

GI, Gastrointestinal; SIADH, syndrome of inappropriate antidiuretic hormone secretion.

(3) Hyperglycemia: Na<sup>+</sup> decreased 1.6 mEq/L for each 100-mg/dL rise in glucose

c. Clinical manifestations: Nausea, headache, lethargy, seizure, coma

2. **Hypernatremia:** Etiologies, diagnostic studies, and management (Table 11-8)

## B. Potassium

### 1. Hypokalemia:

a. Etiologies and laboratory data (Table 11-9)

b. Clinical manifestations: Skeletal muscle weakness or paralysis, ileus, cardiac arrhythmias.<sup>12,13</sup> Electrocardiogram (ECG) changes include delayed depolarization, with flat or absent T waves and, in extreme cases, U waves.

c. Diagnostic studies:

(1) Blood: Electrolytes, blood urea nitrogen/creatinine (BUN/Cr), creatine kinase (CK), glucose, renin, arterial blood gas (ABG)

(2) Urine: Urinalysis, K<sup>+</sup>, Na<sup>+</sup>, Cl<sup>-</sup>, osmolality, 17-ketosteroids

(3) Other: ECG, consider evaluation for Cushing syndrome (Chapter 10)

d. Management: Rapidity of treatment should depend on symptom severity. See Formulary for dosage information:

(1) Acute: Calculate deficit, and replace with potassium acetate or potassium chloride. Enteral replacement is safer when feasible, with less risk for iatrogenic hyperkalemia. Closely follow serum K<sup>+</sup>.

(2) Chronic: Determine daily requirement, and replace with potassium chloride or potassium gluconate.

**TABLE 11-8**

**HYPERNATREMIA**

Decreased Weight		
Renal Losses	Extrarenal Losses	Increased Weight
Nephropathy	GI losses	Exogenous Na <sup>+</sup>
Diuretic use	Skin losses	Mineralocorticoid excess
Diabetes insipidus	Respiratory*	Hyperaldosteronism
Postobstructive diuresis		
Diuretic phase of ATN		
LABORATORY DATA		
↑ Urine Na <sup>+</sup>	↓ Urine Na <sup>+</sup>	Relative ↓ urine Na <sup>+</sup> †
↑ Urine volume	↓ Urine volume	Relative ↓ urine volume
↓ Specific gravity	↑ Specific gravity	Relative ↑ specific gravity
CLINICAL MANIFESTATIONS		
Predominantly neurologic symptoms: lethargy, weakness, altered mental status, irritability, and seizures. <sup>12,13</sup> Additional symptoms may include muscle cramps, depressed deep tendon reflexes, and respiratory failure.		
MANAGEMENT		
Replace free water losses based on calculations in text and treat cause. Consider a natriuretic agent if there is increased weight.		

\*This cause of hypernatremia is usually secondary to free water loss, so the fractional excretion of sodium may be decreased or normal.

†Exogenous Na<sup>+</sup> administration will cause an increase in the fractional excretion of sodium.

ATN, Acute tubular necrosis; GI, gastrointestinal.

**TABLE 11-9**

**CAUSES OF HYPOKALEMIA**

Decreased Stores			
Hypertension	Normal Blood Pressure		Normal Stores*
	Renal	Extrarenal	
Renovascular disease	RTA	Skin losses	Metabolic alkalosis
Excess renin	Fanconi syndrome	GI losses	Hyperinsulinemia
Excess mineralocorticoid	Bartter syndrome	High CHO diet	Leukemia
Cushing syndrome	DKA	Enema abuse	β <sub>2</sub> -Catecholamines
	Antibiotics	Laxative abuse	Familial hypokalemic
	Diuretics	Anorexia nervosa	periodic paralysis
	Amphotericin B	Malnutrition	Familial
LABORATORY DATA			
↑ Urine K <sup>+</sup>	↑ Urine K <sup>+</sup>	↓ Urine K <sup>+</sup>	↑ Urine K <sup>+</sup>

\*Blood pressure may vary.

CHO, Carbohydrate; DKA, diabetic ketoacidosis; GI, gastrointestinal; RTA, renal tubular acidosis.

TABLE 11-10

## CAUSES OF HYPERKALEMIA

Increased Stores		
Increased Urine K <sup>+</sup>	Decreased Urine K <sup>+</sup>	Normal Stores
Transfusion with aged blood	Renal failure	Tumor lysis syndrome
Exogenous K <sup>+</sup> (e.g., salt substitutes)	Hypoadosteronism	Leukocytosis (>100 K/ $\mu$ L)
Spitzer syndrome	Aldosterone insensitivity	Thrombocytosis (>750 K/ $\mu$ L)
	↓ Insulin	Metabolic acidosis*
	K <sup>+</sup> -sparing diuretics	Type IV RTA
	Congenital adrenal hyperplasia	Blood drawing (hemolyzed sample)
		Rhabdomyolysis/crush injury
		Malignant hyperthermia
		Theophylline intoxication

\*For every 0.1-unit reduction in arterial pH, there is an approximately 0.2–0.4 mEq/L increase in plasma K<sup>+</sup>.

RTA, Renal tubular acidosis.

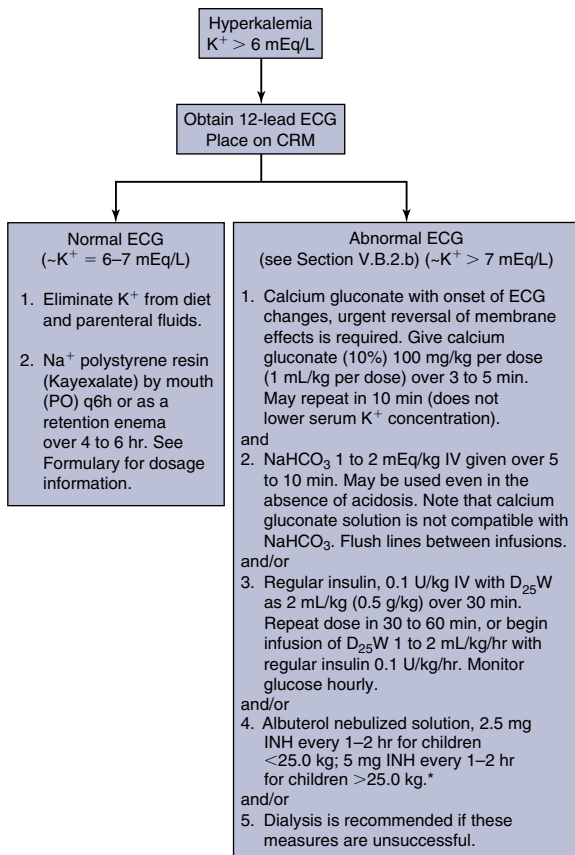
## 2. Hyperkalemia:

- Etiologies (Table 11-10)
- Clinical manifestations: Skeletal muscle weakness, paresthesias, and ECG changes. Typical ECG changes of hyperkalemia progress with increasing serum K<sup>+</sup> values:
  - Peaked T waves
  - Loss of P waves with widening of QRS
  - ST-segment depression with further widening of QRS
  - Bradycardia, atrioventricular (AV) block, ventricular arrhythmias, torsades de pointes, and cardiac arrest
- Management: Stop all IV infusions containing potassium; see algorithm in Fig. 11-3.

## C. Calcium

### 1. Hypocalcemia:

- Etiologies (Box 11-2)
- Clinical manifestations: Tetany, neuromuscular irritability with weakness, paresthesias, fatigue, cramping, altered mental status, seizures, laryngospasm, cardiac arrhythmias<sup>12,13</sup>:
  - ECG changes (prolonged QT interval)
  - Trousseau sign (carpopedal spasm after arterial occlusion of an extremity for 3 minutes)
  - Chvostek sign (muscle twitching with percussion of facial nerve)
- Diagnostic studies:
  - Blood: Total and ionized Ca<sup>2+</sup>, phosphate, alkaline phosphatase, Mg<sup>2+</sup>, total protein, BUN, creatinine, 25-OH vitamin D, parathyroid hormone (PTH):
    - Albumin:  $\Delta$  of 1 g/dL changes total serum Ca<sup>2+</sup> in the same direction by 0.8 mg/dL.
    - pH: Acidosis increases ionized calcium.

**FIGURE 11-3**

Algorithm for hyperkalemia. CRM, cardiorespiratory monitor; D<sub>25</sub>W, 25% dextrose in water; ECG, electrocardiogram; INH, inhaled; IV, intravenous. \*Dosing for Albuterol. In: DRUG-DEX System (Internet database). Greenwood Village, Colo: Thomson Reuters (Healthcare). Updated periodically.

(2) Urine: Ca<sup>2+</sup>, phosphate, creatinine

(3) Other: Chest x-ray (visualize thymus), ankle, and wrist films (assess for rickets), ECG (QT interval)

d. Management: See Formulary for dosing information:

(1) Acute: Consider IV replacement (calcium gluconate, calcium gluceptate, or calcium chloride [cardiac arrest dose]).

(2) Chronic: Consider use of oral supplements of calcium carbonate, calcium gluconate, calcium globionate, or calcium lactate.

## BOX 11-2

## ETIOLOGIES OF HYPOCALCEMIA AND HYPERCALCEMIA

Hypocalcemia	Hypercalcemia
Hypoparathyroidism	Hyperparathyroidism
Vitamin D deficiency	Vitamin D intoxication
Hyperphosphatemia	Excessive exogenous calcium administration
Pancreatitis	Malignancy
Malabsorption states (malnutrition)	Prolonged immobilization
Drugs (anticonvulsants, cimetidine, aminoglycosides, calcium channel blockers)	Thiazide diuretics
Hypomagnesemia/hypermagnesemia	Subcutaneous fat necrosis
Maternal hyperparathyroidism (in neonates)	Williams syndrome
Ethylene glycol ingestion	Granulomatous disease (e.g., sarcoidosis)
Calcitriol (activated vitamin D) insufficiency	Hyperthyroidism
Tumor lysis syndrome	Milk-alkali syndrome

## e. Special considerations:

- (1) Symptoms of hypocalcemia refractory to  $\text{Ca}^{2+}$  supplementation may be caused by hypomagnesemia.
- (2) Significant hyperphosphatemia should be corrected before correction of hypocalcemia, because renal calculi or soft-tissue calcification may occur if  $\text{total } [\text{Ca}^{2+}] \times [\text{PO}_4^{3-}] \geq 55$ .

2. **Hypercalcemia:**

## a. Etiologies (see Box 11-2)

## b. Clinical manifestations: Weakness, irritability, lethargy, seizures, coma, abdominal cramping, anorexia, nausea, vomiting, polyuria, polydipsia, renal calculi, pancreatitis, ECG changes (shortened QT interval)

## c. Diagnostic studies:

- (1) Blood: Total and ionized  $\text{Ca}^{2+}$ , phosphate, alkaline phosphatase, total protein, albumin, BUN, creatinine, PTH, 25-OH vitamin D
- (2) Urine:  $\text{Ca}^{2+}$ , phosphate, creatinine
- (3) Other: ECG (calculate QT interval), kidney, ureter, bladder (KUB) radiograph or renal ultrasound (assess for renal calculi)<sup>14</sup>

## d. Management:

- (1) Treat the underlying disease.
- (2) Hydration: Increase urine output and  $\text{Ca}^{2+}$  excretion. If glomerular filtration rate and blood pressure are stable, give NS with maintenance  $\text{K}^+$  at two to three times maintenance rate until  $\text{Ca}^{2+}$  is normalized.
- (3) Diuresis with furosemide.
- (4) Consider hemodialysis for severe or refractory cases.
- (5) Consider steroids in malignancy, granulomatous disease, and vitamin D toxicity to decrease vitamin D and  $\text{Ca}^{2+}$  absorption (in consultation with appropriate specialists).
- (6) Severe or persistently elevated  $\text{Ca}^{2+}$ : Consider calcitonin or bisphosphonate in consultation with endocrinologist.

## BOX 11-3

## ETIOLOGIES OF HYPOMAGNESEMIA AND HYPERMAGNESEMIA

**Hypomagnesemia****Increased Urinary Losses**

Diuretic use, renal tubular acidosis, hypercalcemia, chronic adrenergic stimulants, chemotherapy

**Increased Gastrointestinal Losses**

Malabsorption syndromes, severe malnutrition, diarrhea, vomiting, short bowel syndromes, enteric fistulas

**Endocrine Etiologies**

Diabetes mellitus, parathyroid hormone disorders, hyperaldosterone states

**Decreased Intake**

Prolonged parenteral fluid therapy with  $Mg^{2+}$ -free solutions

**Hypermagnesemia****Renal Failure****Excessive Administration**

Status asthmaticus, eclampsia/preeclampsia, cathartics, enemas, phosphate binders

**D. Magnesium****1. Hypomagnesemia:**

- Etiologies (Box 11-3)
- Clinical manifestations: Anorexia, nausea, weakness, malaise, depression, nonspecific psychiatric symptoms, hyperreflexia, carpopedal spasm, clonus, tetany, ECG changes (atrial and ventricular ectopy; torsades de pointes)
- Diagnostic studies:
  - Blood:  $Mg^{2+}$ , total and ionized  $Ca^{2+}$
  - Other: Consider evaluation for renal/gastrointestinal losses or endocrine etiologies
- Management: See Formulary for dosing and side effects:
  - Acute: Magnesium sulfate
  - Chronic: Magnesium oxide or magnesium sulfate

**2. Hypermagnesemia:**

- Etiologies (see Box 11-3)
- Clinical manifestations: Depressed deep tendon reflexes, lethargy, confusion, respiratory failure (in extreme cases)

**NOTE:** Neonates born prematurely after tocolysis with magnesium sulfate are at high risk for respiratory sequelae, but serum magnesium levels tend to normalize within 72 hours.

- Diagnostic studies:  $Mg^{2+}$ , total and ionized  $Ca^{2+}$ , BUN, creatinine
- Management:

- Stop supplemental  $Mg^{2+}$
- Diuresis
- $Ca^{2+}$  supplements such as calcium chloride (cardiac arrest doses), or calcium gluconate (see Formulary for dosing)
- Dialysis if life-threatening levels are present

## E. Phosphate

### 1. Hypophosphatemia:

- Etiologies (Box 11-4)
- Clinical manifestations: Symptomatic only at very low levels ( $<1$  mg/dL), with irritability, paresthesias, confusion, seizures, myocardial depression, apnea in very low-birth-weight infants, and coma
- Diagnostic studies
  - Blood: Phosphate, total and ionized  $\text{Ca}^{2+}$ , BUN, creatinine, Na, K,  $\text{Mg}^{2+}$ ; consider PTH and vitamin D
  - Urine:  $\text{Ca}^{2+}$ , phosphate, creatinine, pH
- Management:
  - Insidious onset of symptoms: PO potassium phosphate or sodium phosphate (see Formulary for dosing)
  - Acute onset of symptoms: IV potassium phosphate or sodium phosphate (see Formulary for dosing)

### 2. Hyperphosphatemia:

- Etiologies (see Box 11-4)
- Clinical manifestations: Symptoms of resulting hypocalcemia (see previous)
- Diagnostic studies:
  - Blood: Phosphate, total and ionized  $\text{Ca}^{2+}$ , BUN, creatinine, Na, K,  $\text{Mg}^{2+}$ ; consider PTH, vitamin D, complete blood cell count (CBC), arterial blood gas
  - Urine:  $\text{Ca}^{2+}$ , phosphate, creatinine, urinalysis
- Management:
  - Restrict dietary phosphate.
  - Phosphate binders (calcium carbonate, aluminum hydroxide; use with caution in renal failure). See Formulary for dosing.
  - For cell lysis (with normal renal function), give an NS bolus and IV mannitol. See Chapter 22 for management of tumor lysis syndrome.
  - If patient has poor renal function, consider dialysis.

#### BOX 11-4

##### ETIOLOGIES OF HYPOPHOSPHATEMIA AND HYPERPHOSPHATEMIA

Hypophosphatemia	Hyperphosphatemia
Starvation	Hypoparathyroidism (rarely in the absence of renal insufficiency)
Protein-energy malnutrition	Excessive administration of phosphate (oral, intravenous, or enemas)
Malabsorption syndromes	Tumor lysis syndrome
Intracellular shifts associated with respiratory or metabolic alkalosis	Reduction of glomerular filtration rate to $<25\%$ (may occur at smaller reductions in neonates)
Treatment of diabetic ketoacidosis	
Corticosteroid administration	
Increased renal losses (e.g., renal tubular defects, diuretic use)	
Vitamin D–deficient and vitamin D–resistant rickets	
Very low-birth-weight infants when intake does not meet demand	

## VI. ACID-BASE/OSMOLAR GAP DISTURBANCES

### A. Definitions

1. **Serum osmolality:** Number of dissolved particles per kilogram. Can be calculated as follows:

$$2[\text{serum Na}^+] + \text{glucose (mg/dL)} / 18 + \text{BUN (mg/dL)} / 2.8$$

- a. Normal range: 275–295 mOsm/kg
- b. Serum osmolar gap = calculated serum osmolality – laboratory measured osmolality

**NOTE:** May be elevated in some anion gap acidosis, but a markedly elevated osmolar gap in the setting of an anion gap acidosis is highly suggestive of acute methanol or ethylene glycol intoxication.

2. **Anion gap (AG):** Represents anions other than bicarbonate and chloride required to balance the positive charge of  $\text{Na}^+$ . ( $\text{K}^+$  is considered negligible in AG calculations.)

$$\text{AG} = \text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-) \quad (\text{Normal: } 12 \text{ mEq/L} \pm 2 \text{ mEq/L})$$

- a. The majority of unmeasured anions contributing to the anion gap in normal individuals are albumin and phosphate. A decrease in either of these components will decrease the anion gap and could mask an increase in organic acids such as lactate. Correcting the anion gap for albumin concentration increases the utility of the traditional method. The following equation can be used; AG is measured in mEq/L and albumin is measured in g/dL<sup>15</sup>:
- b. Corrected AG = Observed AG + 2.5 x (Normal albumin – Measured albumin)

3. **Acidosis (pH < 7.35):**

- a. Respiratory acidosis:  $\text{Pco}_2 > 45 \text{ mmHg}$
- b. Metabolic acidosis: Arterial bicarbonate < 22 mmol/L

4. **Alkalosis (pH > 7.45):**

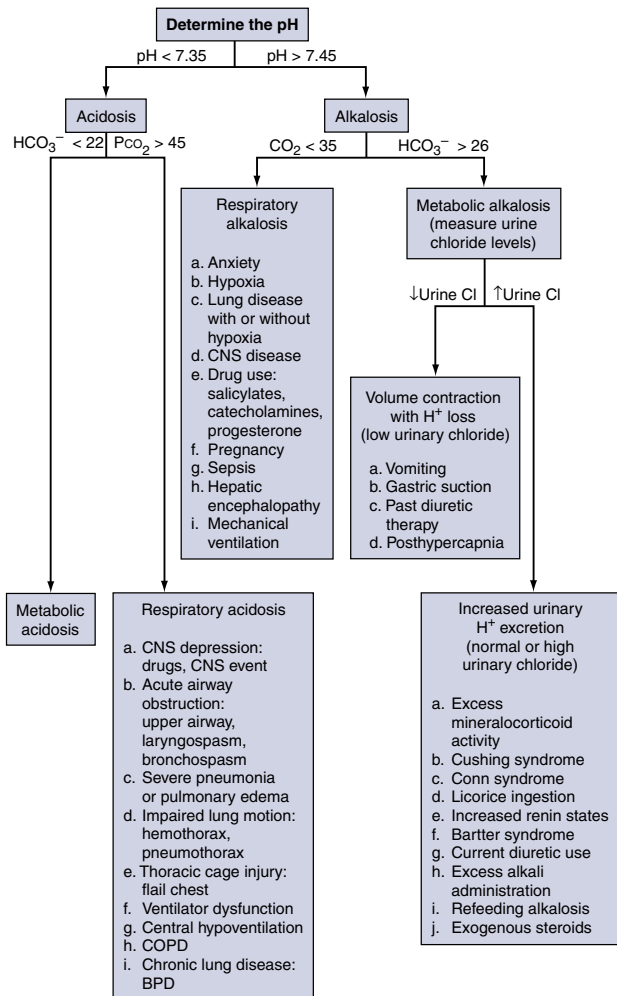
- a. Respiratory alkalosis:  $\text{Pco}_2 < 35 \text{ mmHg}$
- b. Metabolic alkalosis: Arterial bicarbonate > 26 mmol/L

### B. Rules for Determining Primary Acid-Base Disorders (see Table 24-3; Calculation of Expected Compensatory Response)<sup>16</sup>

1. **Determine the pH:** Body does not fully compensate for primary acid-base disorders, so the primary disturbance will shift the pH away from 7.40. Examine the  $\text{Pco}_2$  and  $\text{HCO}_3^-$  to determine whether the primary disturbance is a metabolic acidosis/alkalosis or respiratory acidosis/alkalosis.
2. **Calculate the anion gap:** If anion gap is >20 mmol/L, there is a primary metabolic acidosis regardless of pH or serum bicarbonate concentration. (The body does not generate a large anion gap to compensate for a primary disorder.)

### C. Etiology of Acid-Base Disturbances (Fig. 11-4)



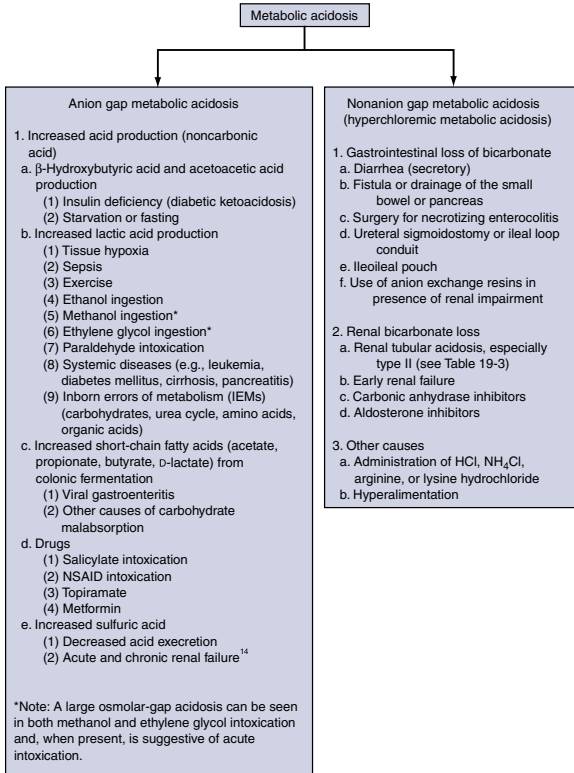


A

FIGURE 11-4

**A and B,** Etiology of acid-base disturbances. BPD, bronchopulmonary dysplasia; CNS, central nervous system; COPD, chronic obstructive pulmonary disease; NSAID, nonsteroidal antiinflammatory drug.

Continued



B

FIGURE 11-4, cont'd

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# Chapter 12

## Gastroenterology

Tina Navidi, MD

 See additional content on Expert Consult

### I. WEBSITES

North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition: [www.naspghan.org](http://www.naspghan.org)

American College of Gastroenterology: [www.acg.gi.org](http://www.acg.gi.org)

### II. GASTROINTESTINAL EMERGENCIES

#### A. Gastrointestinal Bleeding

1. **Presentation**—Blood loss from the gastrointestinal (GI) tract occurs in four ways: Hematemesis, hematochezia, melena, and occult bleeding.
2. **Differential diagnosis of GI bleeding:** [Table 12-1](#).

**TABLE 12-1**

#### DIFFERENTIAL DIAGNOSIS OF GI BLEEDING

Age	Upper GI Tract	Lower GI Tract
Newborns (0–30 days)	Swallowed maternal blood Gastritis	Necrotizing enterocolitis Malrotation with midgut volvulus Anal fissure Hirschsprung disease
Infant (30 days–1 year)	Gastritis Esophagitis Peptic ulcer disease	Anal fissure Allergic proctocolitis Intussusception Meckel diverticulum Lymphonodular hyperplasia Intestinal duplication Infectious colitis
Preschool (1–5 years)	Gastritis Esophagitis Peptic ulcer disease Esophageal varices Epistaxis	Juvenile polyps Lymphonodular hyperplasia Meckel diverticulum Hemolytic-uremic syndrome Henoch-Schönlein purpura Infectious colitis Anal fissure
School age and adolescent	Esophageal varices Peptic ulcer disease Epistaxis Gastritis	Inflammatory bowel disease Infectious colitis Juvenile polyps Anal fissure Hemorrhoids

Modified from Pearl R. The approach to common abdominal diagnoses in infants and children. Part II. *Pediatr Clin North Am*. 1998;45:1287–1326.

### 3. Initial evaluation and management

- a. Assess airway, breathing, circulation, and hemodynamic stability.
- b. Perform physical examination, looking for evidence of bleeding.
- c. Verify bleeding with rectal examination, testing of stool or emesis for occult blood, and/or gastric lavage.
- d. Obtain baseline laboratory tests. Complete blood cell count (CBC), prothrombin time/partial thromboplastin time (PT/PTT), blood type and cross-match, reticulocyte count, blood smear, blood urea nitrogen (BUN)/creatinine, electrolytes, and a panel to assess for disseminated intravascular coagulation (D-dimer, fibrinogen).
- e. Begin initial fluid resuscitation with normal saline or lactated Ringer solution. Consider transfusion if there is continued bleeding, symptomatic anemia, and/or a hematocrit level <20%. Initiate intravenous acid suppression therapy, preferably with a proton pump inhibitor (PPI).
- f. Further evaluation and therapy based on assessment and site of bleeding:
  - (1) + Gastric lavage: consider esophagogastroduodenoscopy (EGD) and testing for *H. Pylori*. Treatment may include histamine-2 (H2) blocker, PPI. (Use nasogastric tube with caution if esophageal varices are suspected.<sup>1</sup>)
  - (2) + Stool hemoccult: Abdominal film, upper GI study ( $\pm$  small bowel follow-through), air-contrast barium enema, colonoscopy, Meckel scan, tagged red cell scan. If signs/symptoms of infection exist, consider stool culture, stool ova and parasites, *Clostridium difficile* toxin.

### B. Acute Abdominal Pain<sup>2</sup>

1. **Definition:** Severe abdominal pain (localized or generalized).<sup>3</sup> May require emergency surgical evaluation/intervention.
2. **Differential diagnosis:** Table 12-2
3. **Evaluation:**
  - a. History: Course and characterization of pain, diarrhea, emesis, melena, hematochezia, fever, last oral intake, emesis, menstrual history, vaginal symptoms, urinary symptoms, and respiratory symptoms. Assess GI history, travel history, and diet.
  - b. Physical examination: Vital signs, toxic appearing, rashes, arthritis, jaundice. Thorough general exam including: Abdominal tenderness on palpation, rebound/guarding, rigidity, masses, distention, change in bowel sounds. Rectal exam with stool Hemoccult test. Pelvic exam (discharge, masses, adnexal/cervical motion tenderness), genital exam.
  - c. Radiologic studies: Obtain plain abdominal radiographs to assess for obstruction, constipation, free air, gallstones, and kidney stones. Consider chest radiograph to evaluate for pneumonia, abdominal/pelvic ultrasonography, abdominal computed tomography (CT) with contrast (include rectal contrast for appendicitis evaluation).
  - d. Laboratory studies to consider: Electrolytes, chemistry panel, CBC, liver and kidney function tests, coagulation studies, blood type and screen/cross-match, urinalysis, amylase, lipase, gonorrhea/chlamydia cultures (or polymerase chain reaction probes), beta-human chorionic

TABLE 12-2

## ACUTE ABDOMINAL PAIN

GI source	Appendicitis, pancreatitis, intussusception, malrotation with volvulus, inflammatory bowel disease, gastritis, bowel obstruction, mesenteric lymphadenitis, irritable bowel syndrome, abscess, hepatitis, perforated ulcer, Meckel diverticulitis, cholecystitis, choledocholithiasis, constipation, gastroenteritis
Renal source	Urinary tract infection, pyelonephritis, nephrolithiasis
Genitourinary (GU) source	Ectopic pregnancy, ovarian cyst/torsion, pelvic inflammatory disease, testicular torsion
Oncologic source	Wilms tumor, neuroblastoma, rhabdomyosarcoma, lymphoma
Other sources	Henoch-Schönlein purpura, pneumonia, sickle cell anemia, diabetic ketoacidosis, juvenile rheumatoid arthritis, incarcerated hernia

gonadotropin ( $\beta$ -hCG), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP)

#### 4. Management:

- Immediate: Make the patient NPO (ensure that they have nothing by mouth). Begin rehydration. Consider nasogastric decompression, serial abdominal examinations, surgical/gynecologic/GI evaluation, pain control, and antibiotics as indicated.

### III. CONDITIONS OF THE GI TRACT (ESOPHAGUS/STOMACH/BOWEL)

#### A. Vomiting

- Definition:** Forceful oral expulsion of gastric contents, can be bilious (green or yellow) or nonbilious
- Diagnosis/evaluation:** Review feeding and medication history. Assess: bilious, hematemesis, acute vs. chronic. Consider: Electrolytes, CBC, UA,  $\beta$ -hCG, pancreatic enzymes. Imaging: Plain abdominal film with upright view (rule out obstruction, free air), abdominal ultrasound, upper GI, neurologic evaluation and imaging. Nasogastric/orogastric tube decompression if GI obstruction suspected. Consider surgical consultation if bilious or hematemesis.
- Differential:** [Table 12-3](#)
- Management:** Hydration. Avoid antiemetic unless specific benign etiology is identified.

#### B. Diarrhea<sup>4</sup>

- Definition:** Usual stool output is 10 g/kg/day in children and 100 g/day in adults. Stool loss of >10 g/kg/day in infants and young children or >200 g/day in older children or adults is considered diarrhea.<sup>5</sup> Acute diarrhea is >3 loose or watery stools per day. Chronic diarrhea is diarrhea lasting more than 14 days.
- Diagnosis/evaluation:** History to assess acute vs. chronic, travel, recent antibiotic use, immune status. Consider laboratory evaluation: Electrolytes, CBC, stool Hemocult, urine culture (young, febrile children), stool culture (febrile  $\pm$  bloody stools), stool tests for leukocytes, *C. difficile*

TABLE 12-3

## DIFFERENTIAL DIAGNOSIS OF VOMITING

Age	Typically Nonbilious	Typically bilious
Newborn & infant (0 days–1 year)	Overfeeding, physiologic reflux, milk protein sensitivity, pyloric stenosis, necrotizing enterocolitis, metabolic disorder, infection (GU, respiratory, GI), esophageal/gastric atresia/stenosis, Hirschsprung disease	Malrotation ± volvulus, intestinal atresia/stenosis, intussusception, pancreatitis
Preschool (1–5 years)	Cyclic vomiting, infectious (GI, GU), toxin ingestion, diabetic ketoacidosis (DKA), central nervous system (CNS) mass effect, eosinophilic esophagitis, posttussive, peptic disease, appendicitis	Malrotation, intussusception, incarcerated hernia, pancreatitis, intestinal dysmotility
School age & adolescent	Eating disorders, pregnancy, CNS mass effect, eosinophilic esophagitis, DKA, peptic disease, cyclic vomiting, toxins/drugs of abuse, infectious (GU, GI), appendicitis	Peritoneal adhesions, incarcerated hernia, pancreatitis, intestinal dysmotility

toxin, ova and parasites, viral antigens (e.g., rotavirus).

3. **Etiology:** Infectious or malabsorptive with osmotic or secretory mechanism

a. Osmotic diarrhea: Water is drawn into intestinal lumen by maldigested nutrients (e.g., celiac or pancreatic disease, lactose) or other osmotic compounds. Stool volume depends on diet and decreases with fasting (stool osmolar gap  $\geq 100$  mOsm/kg).

b. Secretory diarrhea: Water accompanies secreted or unabsorbed electrolytes into the intestinal lumen (e.g., excessive secretion of chloride ions caused by cholera toxin). Stool volume is increased and does not vary with diet (stool osmolar gap  $< 100$  mOsm/kg).

c. Stool osmolar gap = Stool Osm –  $(2 \times [\text{stool } \{Na\}m \text{ Eq/L} + \text{stool } \{K\}m \text{ Eq/L}])$ . Stool Osm is infrequently measured: Standard value is 290 mOsm/kg.<sup>6</sup>

#### 4. Management

a. Oral rehydration therapy (ORT): Mainstay of initial management regardless of etiology. Parenteral hydration is indicated in severe dehydration, hemodynamic instability, or failure of ORT. See Chapter 11 for oral rehydration solutions and calculation of deficit and maintenance fluid requirements.

b. Diet: Restart regular diet once patient is rehydrated, unless found to be the source of the diarrhea (e.g., gluten in celiac disease [CD]).

c. Other: Nonspecific antidiarrheal agents (e.g., adsorbents such as kaolin-pectin), antimotility agents (e.g., loperamide), antisecretory drugs, and toxin binders (e.g., cholestyramine) have limited data regarding efficacy and may adversely affect motility. If infectious, antimicrobial therapy may be indicated. If malabsorptive (e.g., CD, inflammatory bowel disease), therapy should be tailored to disease process.

- d. Probiotics. Evidence supporting use of probiotics (live microorganisms in fermented foods that promote optimal health by establishing improved balance in intestinal microflora) is limited, but efficacy has been demonstrated in the following circumstances: antibiotic-associated diarrhea, mild to moderate acute diarrhea, *C. difficile* diarrhea (severe recurrent disease only), and prevention of atopic dermatitis. Probiotics are not regulated by the U.S. Food and Drug Administration (FDA), so there is no oversight of quality control (including potency).<sup>7</sup>

### C. Constipation and Encopresis<sup>8</sup>

Normal stooling patterns by age: Infants 0–3 months, 2–3 bowel movements (BM)s/day; 6–12 months, 1.8/day; 1–3 years, 1.4/day; >3 years, 1/day

#### 1. Definitions:

- a. **Constipation:** Delay or difficulty in defecation for 2 or more weeks. Functional causes of constipation are most common.

(1) Functional

(2) Nonfunctional: See [Table 12-4](#) for differential diagnosis.

#### (3) Diagnosis/evaluation:

- (a) History: Timing of first meconium stool, family's definition of constipation, duration of condition and age of onset, toilet training experience, frequency/consistency/size of stools, pain or bleeding with defecation, presence of abdominal pain, soiling of underwear, stool withholding behavior, change in appetite, abdominal distention, anorexia, nausea, vomiting, weight loss, or poor weight gain, allergies, dietary history, medications, developmental history, psychosocial history, family history (constipation, thyroid disorders, cystic fibrosis).
- (b) Physical exam: External perineum, perianal exam, and digital anorectal exam. Stool occult blood test for all infants with constipation, any child with abdominal pain, failure to thrive, intermittent diarrhea, or family history of colon cancer or colonic polyps. Fecal impaction may be diagnosed with physical exam (hard mass within abdomen), digital exam (dilated rectal vault filled with stool), and/or abdominal radiography.

#### (4) Treatment of functional constipation:

- (a) Disimpaction (2–5 days)
- (i) Oral/nasogastric approach: Polyethylene glycol electrolyte solutions effective for initial disimpaction. May also use magnesium hydroxide, magnesium citrate, lactulose, sorbitol, senna, or bisacodyl laxatives (avoid magnesium-containing products in infants owing to potential toxicity, beware of overdose in children).
- (ii) Rectal approach: Saline or mineral oil enemas. Avoid soapsuds, tap water, and magnesium enemas because of potential toxicity. Avoid enemas in infants; may use glycerin suppositories. Avoid phosphate-containing products owing



TABLE 12-4

**DIFFERENTIAL DIAGNOSIS OF NON-FUNCTIONAL CONSTIPATION\***

Anatomic malformations	Anal stenosis, anterior displaced anus, imperforate anus, pelvic mass (e.g., sacral teratoma)
Metabolic and GI	Cystic fibrosis, diabetes mellitus, gluten enteropathy, hypercalcemia, hypokalemia, hypothyroidism, multiple endocrine neoplasia type 2B
Neuropathic conditions	Neurofibromatosis, spinal cord abnormalities, spinal cord trauma, static encephalopathy, tethered cord
Intestinal nerve or muscle disorders	Hirschsprung disease, intestinal neuronal dysplasia, visceral myopathies, visceral neuropathies
Abnormal abdominal musculature	Down syndrome, gastroschisis, prune belly
Connective tissue disorders	Ehlers-Danlos syndrome, scleroderma, systemic lupus erythematosus
Drugs	Antacids, anticholinergics, antidepressants, antihypertensives, opiates, phenobarbital, sucralfate, sympathomimetics
Other	Botulism, cow's milk protein intolerance, heavy metal ingestion (lead), vitamin D intoxication

Modified from Constipation Guideline Committee of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. Evaluation and treatment of constipation in infants and children. *J Pediatr Gastroenterol Nutr.* 2006;43:e1-e13.

\*Note: Remember that functional constipation remains the most common cause.

to risk of acute phosphate nephropathy (reported with use of oral sodium phosphate products).

(b) Maintenance therapy (usually 3–12 months): Goal is to prevent recurrence.

- (i) Dietary changes: Increase intake of fluids and absorbable and nonabsorbable carbohydrates to soften stools. A balanced diet that includes whole grains, fruits, and vegetables is recommended. Data are too weak to support a definitive recommendation for fiber supplementation in the treatment of constipation in children.
- (ii) Behavioral modifications: Regular toilet habits, positive reinforcement. Referral to mental health for help with motivational or behavioral concerns.
- (iii) Medications: Polyethylene glycol (osmotic laxatives), lactulose, magnesium hydroxide, or sorbitol recommended. Avoid prolonged use of stimulant laxatives. Discontinue therapy gradually only after return of regular bowel movements with good evacuation.

- (5) **Special considerations in infants <1 year of age:** 2–4 oz of 100% fruit juice (e.g., prune, pear, apple) recommended in younger infants. Barley cereal, sorbitol-containing fruit purees, lactulose can be used in infants taking solid foods. Glycerin suppositories may be useful. Avoid mineral oil, stimulant laxatives, and phosphate enemas.

### D. Inflammatory Bowel Disease (IBD)<sup>9,10</sup>

#### 1. Classification/types:

- a. **Crohn's disease:** Transmural inflammatory process affecting any segment of the GI tract. Abdominal pain in majority of cases. Other common symptoms include weight loss, diarrhea, lethargy, anorexia, fever, nausea, vomiting, growth retardation, malnutrition, delayed puberty, psychiatric symptoms, arthropathy, and erythema nodosum.<sup>10</sup>
- b. **Ulcerative colitis (UC):** Chronic relapsing inflammatory disease of the colon and rectum. Symptoms (present for at least 2 weeks) include gross or occult rectal bleeding, diarrhea, abdominal pain with or around time of defecation. Exclusion of enteric pathogens (e.g., *Salmonella*, *Shigella*, *Yersinia*, *Campylobacter*, *Escherichia coli* O157:H7, *C. difficile*) is necessary.<sup>11</sup> Weight loss, anorexia, lethargy are less common than in Crohn's disease.

#### 2. Evaluation:

- a. Complete history and physical exam, including family history, exposure to infectious agents or antibiotic treatment, assessment of hydration and nutritional status, signs of peritoneal inflammation, signs of systemic chronic disease. Stomatitis, perianal skin tags, fissures, fistulas are suggestive of Crohn's disease. Presence of fever, orthostasis, tachycardia, abdominal tenderness, distention, or masses suggests moderate to severe disease and need for hospitalization.
- b. Laboratory assessment: CBC, ESR, CRP, serum urea and creatinine, serum albumin, liver function tests. IBD is associated with decreased hemoglobin and albumin, rise in platelet count, ESR, CRP (although children with UC may have normal hemoglobin, platelets, and ESR). Anti-neutrophil cytoplasmic antibodies (ANCA) may be elevated in UC. Diagnostic endoscopy is typically used to make diagnosis.

#### 3. Management:

- a. First-line therapy: Corticosteroids, 5-aminosalicylates, antibiotics
- b. Second-line: Immunosuppression includes thiopurines, methotrexate, cyclosporine, tacrolimus, and anti-tumor necrosis factor (TNF) monoclonal antibodies.
- c. Surgical intervention is indicated only after medical management has failed in both Crohn's and UC. In Crohn's, surgery is indicated for localized disease (strictures), abscess, or disease refractory to medical management.

### E. Gastrointestinal Reflux Disease<sup>12</sup>

1. **Definitions:** Gastroesophageal reflux (GER) is passage of gastric contents into the esophagus, and gastroesophageal reflux disease (GERD) is defined as symptoms or complications of GER.
2. **Evaluation/diagnosis:**
  - a. History and physical examination: Usually sufficient to reliably diagnose GER, identify complications, and initiate management.
  - b. Esophageal pH monitoring: Valid and reliable method of measuring acid reflux.

- c. Esophageal impedance monitoring: Combine with esophageal pH monitoring to detect both acid and nonacid reflux with greater sensitivity than pH monitoring alone.<sup>13</sup>

### 3. **Management:**

- a. Diet: Milk protein sensitivity is one cause of unexplained vomiting in formula-fed infants; evidence supports a 2- to 4- week trial of extensively hydrolyzed protein formula. Milk-thickening agents decrease visible regurgitation but do not decrease GER. No evidence to support routine elimination of specific foods to treat GERD in older children.
- b. Lifestyle: Prone or left-side sleeping position, elevation of head of bed may improve GER symptoms in adolescents. Infants up to 12 months should continue to sleep supine—sudden infant death syndrome (SIDS) risk far outweighs benefit of prone or lateral sleeping in GERD. (May consider prone positioning for infants while awake and monitored.) Obesity and large meal volume are associated with increased GER in adults.
- c. Acid-suppressant therapy: Both PPIs and H<sub>2</sub> receptor antagonists (H<sub>2</sub>RAs) are effective in relieving symptoms and promoting mucosal healing. PPIs are superior to H<sub>2</sub>RAs. Smallest effective dose should be used for acid suppression.
- d. Prokinetic therapy: Potential side effects of each currently available prokinetic agent outweigh potential benefits. There is insufficient evidence to support routine use of metoclopramide, erythromycin, bethanechol, or domperidone for GERD.

## F. **Eosinophilic Esophagitis (EE)**<sup>14</sup>

- 1. **Definition:** Symptoms of esophageal dysfunction with  $\geq 15$  eosinophils/high-power field (hpf) on peripheral blood smear, and absence of pathologic GERD as evidenced by lack of responsiveness to high-dose PPI or normal pH monitoring of distal esophagus.
- 2. **Presentation:** Dysphagia, food impaction, chest pain, food refusal or intolerance, GER symptoms, emesis, abdominal pain, failure to thrive. High rate of atopy in children with EE.
- 3. **Diagnosis:** Endoscopy and esophageal biopsy, allergic evaluation for other atopic conditions.
- 4. **Management:** Dietary therapy (elemental formula or removal of specific foods identified by skin prick or atopy patch testing), PPI therapy (as co-treatment), may consider systemic steroids for emergencies (e.g., dysphagia leading to dehydration, weight loss), topical steroids for less severe symptoms (6- to 8- week course of fluticasone or budesonide metered-dose inhaler (MDI) administered orally *without* spacer). Data on use of steroids in EE are limited—recommendation based on expert opinion and current literature.
- 5. **Differential diagnosis** of esophageal eosinophilia: GERD, EE, eosinophilic gastroenteritis, Crohn's disease, connective tissue disease, hypereosinophilic syndrome, infection, drug hypersensitivity.

### G. Celiac Disease<sup>15</sup>

1. **Definition:** An immune-mediated enteropathy caused by a permanent GI tract sensitivity to gluten in genetically susceptible individuals. Increased occurrence in children with type 1 diabetes mellitus, autoimmune thyroiditis, Down syndrome, Turner syndrome, Williams syndrome, selective immunoglobulin (Ig) A deficiency, and in first-degree relatives of those with celiac disease.
2. **Presentation:** Diarrhea, vomiting, abdominal pain, constipation, abdominal distention, failure to thrive. Non-GI symptoms include dermatitis herpetiformis, dental enamel hypoplasia of permanent teeth, osteoporosis, short stature, delayed puberty, and iron deficiency anemia resistant to oral iron.
3. **Diagnosis:** Measure IgA antibody to human recombinant tissue transglutaminase (TTG) and serum IgA (high prevalence of IgA deficiency in celiac disease). Endomysial antibody is subject to interpretation error and adds cost. If there is known selective IgA deficiency and symptoms are suggestive of celiac disease, testing with TTG IgG is recommended. Confirmation requires intestinal biopsy in all cases with findings of villous atrophy as a characteristic histopathologic feature.
4. **Management:** Lifetime gluten-free diet.

## IV. CONDITIONS OF THE LIVER

### A. Liver Function Studies: (Table 12-5)

1. **Synthetic function:** Albumin, prealbumin, PT, activated PTT, cholesterol. Elevated  $\text{NH}_3$  is evidence of decreased ability to detoxify ammonia.
2. **Liver cell injury:** Elevation of aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase.
3. **Cholestasis:** Increased bilirubin, urobilinogen,  $\gamma$ -glutamyltransferase, alkaline phosphatase, 5'-nucleotidase, serum bile acids.

### B. Acute Liver Failure (ALF)<sup>16</sup>

1. **Definition:** Biochemical evidence of liver injury with no history of known chronic liver disease, presence of coagulopathy not corrected by vitamin K administration, and international normalized ratio (INR)  $>1.5$  if patient has encephalopathy or  $>2.0$  if patient does not have encephalopathy. Causes of ALF vary in reversibility (with treatment or withdrawal of offending agent) and age of presentation.
2. **Etiologies** (incidence varies by age):
  - a. Infection: Herpesvirus, hepatitis A, hepatitis B, adenovirus, cytomegalovirus, Epstein-Barr virus, enterovirus, indeterminate
  - b. Vascular: Budd-Chiari syndrome, portal vein thrombosis, veno-occlusive disease, ischemic hepatitis
  - c. Immune dysregulation: Natural killer (NK) cell dysfunction (hemophagocytic lymphohistiocytosis), autoimmune
  - d. Inherited/metabolic: Wilson disease, mitochondrial, tyrosinemia, galactosemia, fatty acid oxidation defect, iron storage disease

TABLE 12-5

## EVALUATION OF LIVER FUNCTION TESTS

Enzyme	Source	Increased	Decreased	Comments
AST/ALT	Liver, heart, skeletal muscle, pancreas, RBCs, kidney	Hepatocellular injury, rhabdomyolysis, muscular dystrophy, hemolysis, liver cancer	Vitamin B <sub>6</sub> deficiency, uremia	ALT more specific than AST for liver, AST > ALT in hemolysis, AST/ALT >2 in 90% of alcohol disorders in adults
Alkaline phosphatase	Osteoblasts, liver, small intestine, kidney, placenta	Hepatocellular injury, bone growth, disease, trauma, pregnancy, familial	Low phosphate, Wilson disease, zinc deficiency, hypothyroidism, pernicious anemia	Highest in cholestatic conditions; must be differentiated from bone source
GGT	Renal tubules, bile ducts, pancreas, small intestine, brain	Cholestasis, newborn period, induced by drugs	Estrogen therapy, artificially low in hyperbilirubinemia	Not found in bone, increased in 90% of primary liver disease, specific for hepatobiliary disease in nonpregnant patient
5'-NT	Intestine, liver cell membrane, brain, heart, pancreas	Cholestasis		Specific for hepatobiliary disease in nonpregnant patient
NH <sub>3</sub>	Bowel flora, protein metabolism	Hepatic disease secondary to urea cycle dysfunction, hemodialysis, valproic acid therapy, urea cycle enzyme deficiency, organic acidemia and carnitine deficiency		Converted to urea in liver

AST/ALT, Aspartate aminotransferase/alanine aminotransferase; 5'-NT, 5'-nucleotidase; GGT,  $\gamma$ -glutamyl transpeptidase; RBCs, red blood cells.

- e. Drugs/toxins: Acetaminophen, anticonvulsants
- f. Other: Unknown, cancer/leukemia
3. **Presentation:** Prodrome of malaise, nausea, emesis, and anorexia. Jaundice and encephalopathy (hyperammonemia, cerebral edema) may be delayed by hours to weeks. Glucose instability with hypoglycemia, coagulopathy.
4. **Evaluation:**
  - a. Clinical: Neurologic status, signs of chronic liver disease, other chronic disease.

**TABLE 12-6**  
**INTERPRETATION OF THE SEROLOGIC MARKERS OF HEPATITIS B IN COMMON SITUATIONS**

Serologic Marker				Interpretation
HBsAg	Total HBcAb	IgM HBcAb	HBsAb	
–	–	–	–	No prior infection, not immune
–	–	–	+	Immune after hepatitis B vaccination (if concentration $\geq 10$ IU/mL or passive immunization from HBIG administration)
–	+	–	+	Immune after recovery from HBV infection
+	+	+	–	Acute HBV infection
+	+	–	–	Chronic HBV infection

HBsAg, Hepatitis B surface antigen; HBcAb, antibody to hepatitis B core antigen; HBsAb, antibody to hepatitis B surface antigen; HBIG, hepatitis B immune globulin.  
From Davis AR, Rosenthal P. Hepatitis B in children. *Pediatr Rev.* 2008;29:111-120.

- b. Laboratory: Electrolytes, BUN, creatinine, blood glucose, calcium, magnesium, phosphorous, blood gas, CBC with peripheral smear, reticulocyte count, liver function/production (albumin, aspartate aminotransferase [AST], alanine aminotransferase [ALT], alkaline phosphatase), INR, PT, PTT, ammonia, factors V, VII (depleted first in ALF), VIII, fibrinogen. Urine toxicology screen, serum acetaminophen level. Consider viral studies.
- NOTE:** See Table 12-6 for interpretation of serologic markers of hepatitis B.
- c. Imaging: Abdominal ultrasound with Doppler flows, head CT scan to exclude hemorrhage/edema, chest radiograph.
- d. Studies to explore causation: Viral studies, immune function, metabolic studies, tissue biopsies.

**C. Hyperbilirubinemia<sup>17,18</sup>**

Bilirubin is the product of hemoglobin metabolism. There are two forms: Direct (conjugated) and indirect (unconjugated). Hyperbilirubinemia is usually the result of increased hemoglobin load, reduced hepatic uptake, reduced hepatic conjugation, or decreased excretion. Direct hyperbilirubinemia is defined as direct bilirubin >20% of total or direct bilirubin >2 mg/dL. See Table 12-7 for differential diagnosis of hyperbilirubinemia. Refer to Chapter 18 for evaluation and treatment of neonatal hyperbilirubinemia.

**V. PANCREATITIS<sup>19,20</sup>**

Inflammatory disease of the pancreas; falls into two major categories, acute and chronic.

**A. Acute Pancreatitis**

1. **Presentation:** Sudden onset of abdominal pain associated with rise of pancreatic digestive enzymes in serum or urine, with or without

TABLE 12-7

## DIFFERENTIAL DIAGNOSIS OF HYPERBILIRUBINEMIA

INDIRECT HYPERBILIRUBINEMIA	
Transient neonatal jaundice	Breast milk jaundice, physiologic jaundice Polycythemia, reabsorption of extravascular blood
Hemolytic disorders	Autoimmune disease, blood group incompatibility, hemoglobinopathies, microangiopathies, red cell enzyme deficiencies, red cell membrane disorders
Enterohepatic recirculation	Cystic fibrosis, Hirschsprung disease, ileal atresia, pyloric stenosis
Disorders of bilirubin metabolism	Acidosis, Crigler-Najjar syndrome, Gilbert syndrome, hypothyroidism, hypoxia
Miscellaneous	Dehydration, drugs, hypoalbuminemia, sepsis
DIRECT HYPERBILIRUBINEMIA	
Biliary obstruction	Biliary atresia, choledochal cyst, fibrosing pancreatitis, gallstones or biliary sludge, inspissated bile syndrome, neoplasm, primary sclerosing cholangitis
Infection	Cholangitis, cytomegalovirus, Epstein-Barr virus, herpes simplex virus, histoplasmosis, HIV, leptospirosis, liver abscess, sepsis, syphilis, toxocariasis, toxoplasmosis, tuberculosis, urinary tract infection, varicella-zoster virus, viral hepatitis
Genetic/metabolic disorders	$\alpha_1$ -Antitrypsin deficiency, Alagille syndrome, Caroli disease, cystic fibrosis, Dubin-Johnson syndrome, galactokinase deficiency, galactosemia, glycogen storage disease, hereditary fructose intolerance, hypothyroidism, Niemann-Pick disease, rotor syndrome, tyrosinemia, Wilson disease
Chromosomal abnormalities	Trisomy 18, Trisomy 21, Turner syndrome
Drugs	Acetaminophen, aspirin, erythromycin, ethanol, iron, isoniazid, methotrexate, oxacillin, rifampin, steroids, sulfonamides, tetracycline, vitamin A
Miscellaneous	Neonatal hepatitis syndrome, parenteral alimentation, Reye syndrome

radiographic changes in the pancreas. Reversible process. Most common etiologies: Trauma, multisystem disease, drugs, infections, idiopathic, and congenital anomalies. See Table 12-8 for conditions associated with acute pancreatitis.

## 2. Diagnosis/evaluation:

- Clinical signs/symptoms: Abdominal pain (sudden or gradual, most commonly epigastric), anorexia, nausea, vomiting, tachycardia, fever, hypotension, guarding/rebound tenderness/decreased bowel sounds, sonographic or radiologic evidence of pancreatic inflammation. Grey-Turner and Cullen signs are rare in children.
- Laboratory findings:
  - (1) Elevated lipase and amylase:  $\geq 3$  times above normal limit (but no correlation with disease severity). Lipase is more sensitive and specific for acute pancreatitis but normalizes more slowly, so it may be preferable to follow amylase after establishing diagnosis.<sup>9</sup>

**TABLE 12-8**

**CONDITIONS ASSOCIATED WITH ACUTE PANCREATITIS**

<b>SYSTEMIC DISEASES</b>	
Infections	Coxsackie, CMV, cryptosporidium, EBV, hepatitis, influenza A or B, leptospirosis, mycoplasma, mumps, rubella, typhoid fever, varicella
Inflammatory and vasculitic disorders	Collagen vascular diseases, hemolytic uremic syndrome, Henoch-Schönlein purpura, IBD, Kawasaki disease
Sepsis/peritonitis/shock	
Transplantation	
<b>IDIOPATHIC (UP TO 25% OF CASES)</b>	
<b>MECHANICAL STRUCTURAL</b>	
Trauma	Blunt trauma, child abuse, ERCP
Perforation	
Anomalies	Annular pancreas, choledochal cyst, pancreatic divisum, stenosis, other
Obstruction	Parasites, stones, tumors
<b>METABOLIC AND TOXIC FACTORS</b>	
Cystic fibrosis	
Diabetes mellitus	
Drugs/toxins	Salicylates, cytotoxic drugs (L-asparaginase), corticosteroids, chlorothiazides, furosemide, oral contraceptives (estrogen), tetracyclines, sulfonamides, valproic acid, azathioprine, 6-mercaptopurine
Hypercalcemia	
Hyperlipidemia	
Hypothermia	
Malnutrition	
Organic acidemia	
Renal disease	

CMV, Cytomegalovirus; EBV, Epstein-Barr virus; ERCP, endoscopic retrograde cholangiopancreatography.

Modified from Robertson MA. Pancreatitis. In: Walker WA et al, eds. *Pediatric Gastrointestinal Disease*. 3rd ed. New York: BC Decker, 2000:1321-1344; and Werlin SL. Pancreatitis. In: McMillan JA et al, eds. *Oski's Pediatrics*. Philadelphia: Lippincott Williams & Wilkins, 2006:2010-2012.

(2) Additional findings: leukocytosis, hyperglycemia, glucosuria, hypocalcemia, hyperbilirubinemia.

**3. Management:**

- a. Pancreatic rest: Nasogastric decompression, analgesia, intravenous fluid hydration, oral intake restriction. Enteral feeding via nasojejunal tube may be used for nutrition. (In adults, enteral nutrition is associated with lower incidence of infection, surgical intervention, and shorter hospital stay. Minimal pediatric evidence available.)
- b. Antibiotics are reserved for only the most severe cases.

**B. Chronic Pancreatitis**

- 1. **Definition:** Progressive inflammatory process causing irreversible changes in the architecture and function of the pancreas. Common



complications include chronic abdominal pain, loss of exocrine function (malabsorption, malnutrition) and/or endocrine function (diabetes mellitus). Two major morphologic forms: calcific and obstructive (Table EC 12-A).

2. **Management:** (For acute exacerbations) same as management of acute pancreatitis. See Section V.A.3.

### C. Miscellaneous Tests

For descriptions, see Expert Consult.

#### 1. Occult blood

- a. Purpose: To screen for presence of blood through detection of heme in stool
- b. Method: Smear a small amount of stool on test areas of an occult blood test card and allow to air dry. Apply developer as directed.
- c. Interpretation: Blue color resembling that of the control indicates presence of heme. Brisk transit of ingested red meat and inorganic iron may yield a false-positive result. Fruits and vegetables associated with false-positive results include cantaloupes, radishes, bean sprouts, cauliflower, broccoli, and grapes. Screening for presence of blood in gastric aspirates or vomitus should be performed using Gastrocult, not stool Hemocult, cards.

#### 2. Quantitative fecal fat

- a. Purpose: To screen for fat malabsorption by quantitating fecal fat excretion.
- b. Method: Patient should be on a normal diet (35% fat) with amount of calories and fat ingested recorded for 2 days before test and during the test itself. Collect and freeze all stools passed within 72 hours, send to laboratory for determination of total fecal fatty acid content.
- c. Interpretation
  - (1) Total fecal fatty acid excretion of >5 g fat per 24 hours may suggest malabsorption. Results will vary with amount of fat ingested, and normal values have not been established for children <2 years of age.
  - (2) Coefficient of absorption (CA) is a more accurate indicator of fat malabsorption and does not vary with fat intake:

$$CA = \frac{(\text{Grams of fat ingested} - \text{Grams of fat excreted})}{(\text{Grams of fat ingested})} \times 100$$

Infants <6 months of age should absorb >85% of fat intake. By age 1 year, fat absorption should be at an adult level of >95%. Quantitative fecal fat is recommended over qualitative methods (e.g., staining with Sudan III), which depend on spot checks and are thus unreliable for diagnosing fat malabsorption.

TABLE EC 12-A

PROPOSED ETIOLOGIES OF CHRONIC PANCREATITIS IN CHILDHOOD<sup>19,20</sup>

Calcific	Cystic fibrosis, hereditary pancreatitis (e.g., <i>PRSS1</i> and <i>SPINK1</i> mutations), hypercalcemia, hyperlipidemia, idiopathic, juvenile tropical pancreatitis
Obstructive (noncalcific)	Congenital anomalies, idiopathic fibrosing pancreatitis, renal disease, sclerosing cholangitis, sphincter of Oddi dysfunction, trauma

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# Chapter 13

## Genetics: Metabolism and Dysmorphology

*Jessica Duis, MD*

Continuous technologic advances make genetics a constantly evolving field. It is best discussed in separate sections entitled "Metabolism" and "Dysmorphology." When considering a particular diagnosis, a complete patient history should include details of the conception, pregnancy, prenatal ultrasound findings, delivery, postnatal growth, development, a three-generation family history in the form of a pedigree, and a comprehensive physical examination.

### I. WEBSITES/DATABASES

Online Mendelian Inheritance in Man (OMIM): <http://omim.org> (includes a search engine for identifying genetic diseases based on clinical phenotype, gene, and OMIM number)

GeneReviews: [www.genereviews.org](http://www.genereviews.org); expert-authored and peer-reviewed descriptions of inherited disorders

National Newborn Screening and Genetics Resource Center: [genes-r-us.uthscsa.edu/resources.htm](http://genes-r-us.uthscsa.edu/resources.htm)

GeneTests: [www.genetests.org](http://www.genetests.org) (includes information on genetic diagnostic tests, genetic clinics in the United States and laboratories that perform genetic testing)

American College of Medical Genetics: [www.acmg.net/resources/policies/ACT/condition-analyte-links.htm](http://www.acmg.net/resources/policies/ACT/condition-analyte-links.htm) (includes ACT sheets and algorithm to help guide physicians after a positive newborn metabolic screen)

National Organization for Rare Disorders: [www.rarediseases.org](http://www.rarediseases.org)

### II. METABOLISM

#### A. Newborn Metabolic Screening<sup>1-3</sup>

1. **Overview by state:** <http://genes-r-us.uthscsa>

2. **Timing:**

- First screen should be performed within the first 48–72 hours of life (at least 24 hours after initiation of feeding).
- Second screen (requested in some states) should be performed between 1 and 4 weeks of age (after 7 days).
- Preterm infants: Perform initial screen at birth (to collect DNA before transfusions), another at 48–72 hours of age, a third at 7 days of age, and a final at 28 days or before discharge (whichever comes first).

3. **Abnormal results:**

- Requires immediate follow-up and confirmatory testing; consult a geneticist.

- b. ACT Sheets and Confirmatory Algorithms are available for more information on how to proceed with specific abnormalities: [www.acmg.net/resources/policies/ACT/condition-analyte-links.htm](http://www.acmg.net/resources/policies/ACT/condition-analyte-links.htm).

### B. Clinical Presentation<sup>1,4,5</sup> (Box 13-1)

1. **Neonatal:** After appearing well for a brief period of time, which can range from hours to a usual time frame of about 48–72 hours; illness often mistaken for sepsis develops and can progress to coma.
2. **Infancy:** Failure to thrive, poor feeding with vomiting, often presents at the time of intercurrent illness or when the infant begins fasting overnight (usually 7–12 months of age).
3. **Children and adults:** Often a presentation at the time of intercurrent illness; waxing and waning consciousness that may progress to coma.

### C. Evaluation<sup>1,5</sup>

1. **Initial laboratory tests:** Complete metabolic panel (CMP), blood glucose, venous blood gas (VBG), ammonia, lactate, creatine kinase (CK), complete blood cell count (CBC) with differential, urine ketones (Box 13-2).
2. **If metabolic disease is suspected:** Consult a geneticist. General metabolic workup includes plasma amino acids (PAA), urine organic acids (UOA), acylcarnitine profile, quantitative plasma carnitine, lactate/pyruvate (refer to Table 13-1 for collection information).
3. **Special considerations:**<sup>5-7</sup>
  - a. Hyperammonemia: VBG, UOA, PAA, acylcarnitine profile, urine orotic acid (Fig. 13-1)
  - b. Hypoglycemia: During acute illness consider urine ketones, acylcarnitine profile, PAA, UOA, insulin, growth hormone, cortisol, C-peptide (Fig. 13-2)<sup>8</sup>
  - c. Metabolic acidosis: Ammonia, lactic acid, UOA, UA with urine pH, CMP (Fig. 13-3)

#### BOX 13-1

##### WHEN TO SUSPECT METABOLIC DISEASE<sup>1,5</sup>

Overwhelming illness in the neonatal period  
Vomiting  
Acute acidosis, anion gap  
Massive ketosis  
Hypoglycemia  
Coagulopathy  
Deep coma  
Seizures, especially myoclonic  
Hypotonia  
Unusual odor of urine  
Extensive dermatosis, especially monilial  
Neutropenia, thrombocytopenia, or pancytopenia  
Family history of siblings dying early

**BOX 13-2****INITIAL LABORATORY INVESTIGATIONS<sup>4,5</sup>****BLOOD**

Complete metabolic profile (special attention to bicarbonate and anion gap)

Blood glucose

Venous blood gas: pH, Pco<sub>2</sub>, HCO<sub>3</sub>, Po<sub>2</sub>

Ammonia

Lactate

Creatine kinase

Complete blood cell count with differential

Plasma amino acids

Quantitative carnitine

Acylcarnitine profile

**URINE**

Ketones

Urinalysis

Reducing substances

Urine organic acids

**TABLE 13-1****SAMPLE COLLECTION**

Specimen Name	Volume (mL)	Tube	Handling Instructions
Chromosome microarray (SNP array)	2–5	Purple top	Do not freeze, may refrigerate.
Karyotype	2–5	Green top	Room temperature.
DNA-based testing	5–10	Purple top	Room temperature; ship in insulated container overnight.
Plasma ammonia	1–3	Purple top	Place on ice and transport immediately to laboratory.
Plasma amino acids	1–3	Green top	Take to laboratory immediately on ice; if must store, spin down and separate plasma and store at –20°C.
Quantitative carnitine (free and total carnitine)	1–3	Green top	Transport on ice.
Acylcarnitine profile	0.5–2.0	Green top	Transport on ice.
Lactate	2–3	Gray top	Immediately transport on ice.
Urine organic acids	3–5	Urine specimen container	Take immediately to laboratory on ice; if must store, store at –20°C.
Urine amino acids	1–5	Urine specimen container	Take immediately to laboratory on ice; if must store, store at –20°C.

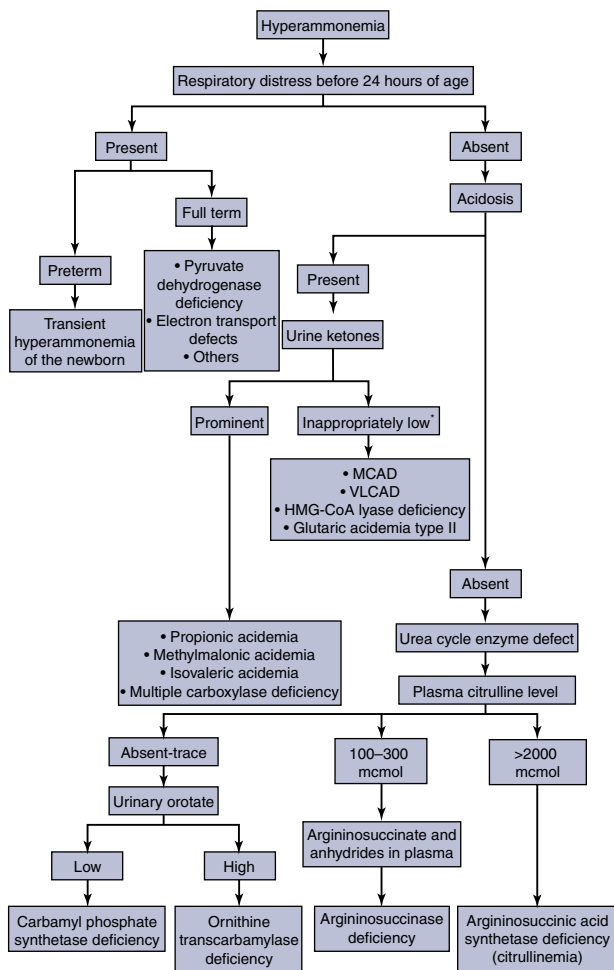
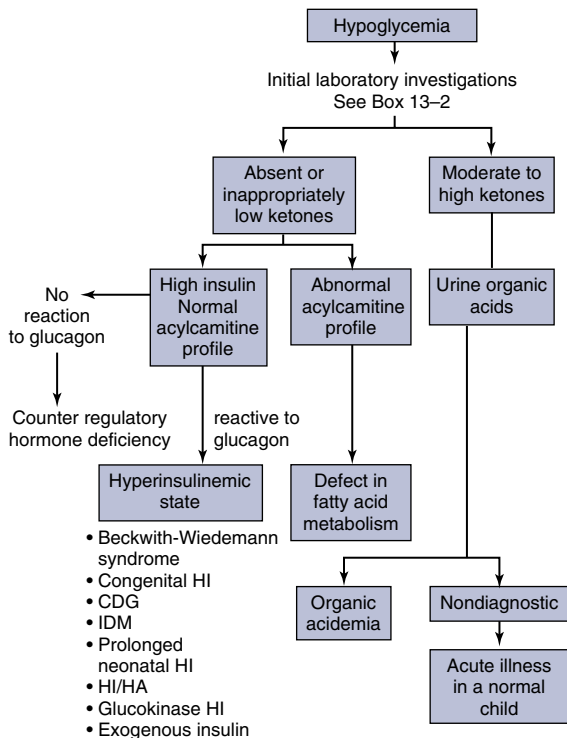


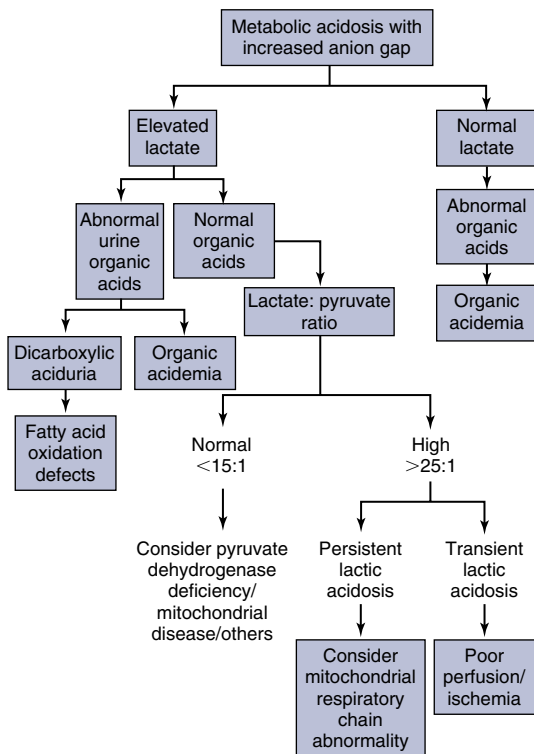
FIGURE 13-1

Differential diagnosis of hyperammonemia. \*Indicates inappropriately low urinary ketones in the setting of symptomatic hypoglycemia. HMG-CoA, Hydroxymethylglutaryl-CoA; MCAD, medium-chain acyl-CoA dehydrogenase; SCAD, short-chain acyl-CoA dehydrogenase; VLCAD, very long-chain acyl-CoA dehydrogenase.<sup>4,5</sup>



**FIGURE 13-2**

B-W, Beckwith-Wiedemann syndrome; CDG, congenital disorder of glycolization; HI, hyperinsulinism; HI/HA, hyperinsulinism/hyperammonemia; IDM, infant of a diabetic mother. (Modified from Burton BK. *Inborn errors of metabolism in infancy: a guide to diagnosis*. Pediatrics. 1998;102:E69; and Cox GF. *Diagnostic approaches to pediatric cardiomyopathy of metabolic genetic etiologies and their relation to therapy*. Prog Pediatr Cardiol. 2007;24:15-25.)

**FIGURE 13-3**

Metabolic acidosis with increased anion gap. (From Burton B. *Inborn errors of metabolism in infancy: a guide to diagnosis*. Pediatrics. 1998;102:E69.)

- d. Neonatal seizures: CSF and plasma amino acids (done simultaneously to determine the glycine ratio to evaluate for nonketotic hyperglycinemia), CSF/serum glucose ratio, neurotransmitters, very long-chain fatty acids, organic acids, serum uric acid, urine sulfites. Consider trial of pyridoxine (100 mg intravenously [IV]), pyridoxal phosphate (30 mg/kg), and folinic acid (3 mg/kg) IV if uncontrollable.
- e. Urine reducing substances (finding with differential):
  - (1) Galactose: Galactosemia
  - (2) Fructose: Hereditary fructose intolerance, fructosuria
  - (3) Glucose: Diabetes mellitus, renal tubular defect
  - (4) Xylose: Pentosuria

- (5) P-hydroxyphenylpyruvic acid: Tyrosinemia
- (6) False positive: Cephalosporins, nalidixic acid

#### D. Treatment of Metabolic Crisis<sup>5-7</sup>

##### 1. Initial intervention:

- a. Normal saline (NS) bolus, 10–20 mL/kg
- b. Start 10% dextrose (D<sub>10</sub>) + 1/4 to 1/2 NS + KCl (10–20 mEq/L) at 1.5–2 times maintenance rate.
- c. Patient should have nothing by mouth except in the diagnosis of Maple Syrup Urine Disease (MSUD). In MSUD it is essential to continue synthetic protein formula to give amino acids that can compete with elevated leucine for the blood brain barrier to prevent cerebral edema.
- d. Bicarbonate should be included in the fluids, equivalent to the patient's home dose or if pH is <7.1.

- 2. **Hemodialysis** should be initiated as soon as possible in infants with hyperammonemia > 250, and patients with any small-molecule disease that is unresponsive to initial management.

##### 3. Commonly used medications:

- a. Carnitine 50 mg/kg/dose IV Q6 hr when ill, or 100 mg/kg/day orally (PO) divided Q8 hr when well.
- b. Sodium phenylacetate/sodium benzoate should be combined with arginine HCl in a 10% dextrose solution to treat acute hyperammonemia in a urea cycle patient. The dose of the sodium phenylacetate / sodium benzoate is 250 mg/kg for a child <20 kg, and 5.5 gm/m<sup>2</sup> for a child >20 kg. The arginine HCl is 2–6 gm/m<sup>2</sup>, depending on the diagnosis (2 gm/m<sup>2</sup> for CPS and OTC; 4–6 gm/m<sup>2</sup> for Citrullinemia; 6 gm/m<sup>2</sup> alone for Argininosuccinase deficiency). As all of these medications have significant side effects and narrow therapeutic windows. Treatment should always be undertaken in consultation with a biochemical geneticist.
- c. Arginine HCl IV for MELAS stroke-like episode.
- d. Sodium benzoate for NKH

#### E. Some Common Metabolic Diseases in Brief<sup>1,4-7</sup>

##### 1. Fatty acid oxidation (FAO) disorders:

- a. Epidemiology: 1/10,000; autosomal recessive disorders:
  - (1) Most common is medium-chain acyl-CoA dehydrogenase (MCAD).
  - (2) Short-chain acyl-CoA dehydrogenase (SCAD) deficiency is picked up on newborn screen, but most patients have no problems even during intercurrent illness.
- b. Presentation:
  - (1) Hypoketotic hypoglycemia, lethargy, coma, vomiting
  - (2) Disorders of long chains can present with rhabdomyolysis and/or cardiomyopathy
- c. Diagnostic evaluation: Blood glucose, urine ketones, complete metabolic panel (CMP), VBG, creatine kinase (CK), ammonia, acylcarnitine profile, quantitative carnitine

## d. Acute management:

- (1) Bolus  $D_{10}$  2 mL/kg in hypoglycemia and/or NS 20 mL/kg for volume repletion.
- (2) Start  $D_{10}$ + 1/4 NS + KCl (based on serum level of K) and run at 1.5–2 times maintenance fluid rate.
- (3) Treat fever aggressively with antipyretics, and treat intercurrent infection.

## e. Chronic management:

- (1) Carnitine supplementation for primary carnitine deficiencies and MCAD (avoid in very long-chain acyl-CoA dehydrogenase [VLCAD] and long-chain 3-hydroxyl-CoA dehydrogenase [LCHAD] disorders).
- (2) In disorders of very long-chain fatty acids, limit intake to low-fat foods and supplementation with medium-chain triglyceride oil.
- (3) In all FAO patients with mild intercurrent illness or decreased day-time intake, nighttime feeds Q4 hr are necessary.

2. **Organic acidemias:**

## a. Epidemiology: All autosomal recessive:

- (1) 3-methylcrotonyl-CoA carboxylase deficiency (3-MCC): 1/15,000 (picked up on newborn screen, but most children are normal without problems during illness)
- (2) Glutaric acidemia type 1 (GA1): 1/30,000–40,000
- (3) Methylmalonic acidemia (MMA): 1/100,000
- (4) Propionic acidemia (PA): 1/150,000
- (5) Isovaleric acidemia: 1/150,000
- (6) Maple syrup urine disease (MSUD): 1/150,000

## b. Presentation:

- (1) Neonatal: Well, full-term infant who develops lethargy, irritability, seizures, hypotonia, poor feeding, hypoglycemia, vomiting
- (2) Older infant/child: Failure to thrive, vomiting, global developmental delays, choreoathetoid or dystonic movements secondary to metabolic stroke in the basal ganglia, bone marrow suppression, frequent infections, pancreatitis, cardiomyopathy

## c. Diagnostic evaluation: Blood glucose, complete metabolic profile, urinalysis to look for infection and ketones, CBC with differential, VBG, ammonia, acylcarnitine profile, PAA, quantitative carnitine

## d. Acute management:

- (1) Start infusion of  $D_{10}$ + 1/4 NS + KCl at 1.5–2 times maintenance
- (2) May need bicarbonate, especially if on it daily at baseline
- (3) Stop all protein feeds (except in MSUD, where synthetic formula should be used at all times if possible)
- (4) Carnitine 50 mg/kg IV Q6 hr in MMA, PA
- (5) 10% glycine 500 mg/kg/day in isovaleric acidemia

## e. Chronic Management: Formula that appropriately restricts amino acids; treatment with carnitine

3. **Urea cycle defects:**

## a. Epidemiology: 1/30,000. Autosomal recessive, except for ornithine transcarbamylase (OTC) deficiency which is X-linked.

- (1) Most common is OTC deficiency.
- (2) OTC deficiency and carbamyl phosphate synthetase (CPS) deficiency are not picked up on newborn screening because it is difficult to distinguish between low and normal citrulline levels.
- b. Presentation: Episodes of acute decompensation characterized by hyperammonemia, lethargy, seizures, coma, respiratory alkalosis, failure to thrive, poor appetite, vomiting, psychosis
- c. Diagnostic evaluation: CMP, VBG, ammonia, PAA, urine orotic acid, urinalysis, CBC to determine if evidence for a bacterial infection.
- d. Acute management:
  - (1) Start IV fluids as per above, stop all protein intake, dialysis as indicated for ammonia > 250
  - (2) Sodium benzoate/sodium phenylacetate and arginine IV
- e. Chronic management: Sodium phenylbutyrate or glycerol phenylbutyrate, citrulline (for OTC deficiency and CPS deficiency), arginine (for citrullinemia and argininosuccinate lyase deficiency), protein-restricted diet
4. **Phenylketonuria (PKU):**
  - a. Epidemiology: Autosomal recessive, 1/10,000–15,000
  - b. Presentation: Intellectual disability if untreated
  - c. Diagnostic evaluation: Most infants diagnosed by newborn screening before clinical appearance; PAA to look at phenylalanine
  - d. Acute management: Phenylalanine-restricted diet
  - e. Chronic management: Phenylalanine-restricted diet; sapropterin effective in a subset of patients at a dose of 10–20 mg/kg/day
5. **Hereditary tyrosinemia (HT1):**
  - a. Epidemiology: Autosomal recessive, 1/100,000
  - b. Presentation: Severe liver failure, vomiting, bleeding, sepsis, hypoglycemia, renal tubulopathy (Fanconi syndrome). Chronic HT1 leads to cirrhosis, failure to thrive, rickets, neuropathy, tubulopathy, neurologic crises
  - c. Diagnostic evaluation: Complete metabolic panel, coagulation studies, CBC with differential, urine organic acids to quantitate succinylacetone, PAA
  - d. Acute management: Management of bleeding complications and providing replacement factors: 2-(2-nitro-4-trifluoromethyl-benzoyl)-1,3-cyclohexanedione (NTBC), 1–2 mg/kg divided twice daily
  - e. Chronic management: Tyrosine- and phenylalanine-restricted diet, NTBC 1–2 mg/kg divided twice daily
6. **Mitochondrial diseases:**<sup>6,9</sup>
  - a. Epidemiology: 1/8500; can be caused by mutations in nuclear or mitochondrial DNA.
  - b. Presentation: Can involve any organ system; symptoms usually neurologic and myopathic. For in-depth discussion, access gene review at [www.ncbi.nlm.nih.gov/books/NBK1224/](http://www.ncbi.nlm.nih.gov/books/NBK1224/).
  - c. Diagnostic evaluation: CMP, CK, VBG, CBC with differential, lactate/pyruvate, CSF levels of lactate/pyruvate, plasma and CSF amino acids, urine organic acids, urine amino acids, brain imaging, mitochondrial DNA testing. Muscle biopsy is no longer indicated except in the case of severe myopathy.

- d. Acute management: ABCs, supportive therapy, encourage anaerobic metabolism.
- e. Chronic management: Cocktail of antioxidants, vitamins, and cofactors.
- 7. **Lysosomal storage diseases:**<sup>10</sup>
  - a. Epidemiology:
    - (1) Mucopolysaccharidosis type I (Hurler syndrome, MPS I): 1/100,000; autosomal recessive
    - (2) Mucopolysaccharidosis type II (Hunter syndrome, MPS II): 1/140,000; X-linked recessive
    - (3) Mucopolysaccharidosis type III (Sanfilippo syndrome, MPS III): 1/100,000; autosomal recessive
    - (4) Mucopolysaccharidosis type IV (Morquio syndrome, MPS IV): 1/75,000-300,000; autosomal recessive
    - (5) Mucopolysaccharidosis type VI (Maroteaux-Lamy syndrome, MPS VI): 1/200,000-300,000; autosomal recessive
    - (6) Mucopolysaccharidosis type VII (Sly syndrome, MPS VII): Rare
  - b. Presentation:
    - (1) Infants normal at birth, except in Sly syndrome (MPS VII), where infants usually die from hydrops.
    - (2) Coarsening of facial features noted at about age 1 year. Progressive dysostosis multiplex, growth failure, hepatomegaly, deafness, psychomotor retardation, intellectual disability, hearing loss.
    - (3) Hurler syndrome (MPS I): Lethal by 10 years of age if not treated with bone marrow transplantation
    - (4) Sanfilippo syndrome (MPS III): Patients aggressive with extremely hyperkinetic behavior and tetraspasticity
    - (5) Morquio syndrome (MPS IV): Small stature with severe skeletal abnormalities
    - (6) Maroteaux-Lamy syndrome (MPS VI): Visceral involvement, normal intelligence
  - c. Diagnostic evaluation: CBC with differential, skeletal survey for dysostosis, specific enzyme activity
  - d. Acute management: Supportive therapy
  - e. Chronic management:
    - (1) Hurler syndrome (MPS I): Stem cell transplantation before 2 years of age may slow progression of cognitive decline but does not affect skeletal manifestations or corneal clouding
    - (2) Maroteaux-Lamy syndrome (MPS VI): Enzyme replacement
    - (3) Non-neuronopathic Hunter syndrome (MPS II): Enzyme replacement
- 8. **Disorders of carbohydrate metabolism—galactosemia:**
  - a. Epidemiology: Galactosemia, 1/30,000; autosomal recessive.
  - b. Presentation:
    - (1) Presents at 3–4 days of life with hypoglycemia, jaundice, diarrhea, hepatomegaly, hyperammonemia, poor feeding, vomiting. Other

presenting symptoms include failure to thrive, lethargy, seizures, cataracts, hepatic failure, and renal failure.

- (2) Galactosemia should be considered in an infant with overwhelming *Escherichia coli* sepsis.

c. Diagnostic evaluation: Galactosemia often made on newborn screening. Obtain blood glucose, comprehensive metabolic panel, ammonia, coagulation studies, urine for reducing substances, galactitol, erythrocyte galactose-1-phosphate, galactose-1-phosphate uridylyltransferase (GALT) activity.

d. Acute management: ABCs, discontinue feeds, dextrose containing fluids.

e. Chronic management: Lactose-free and galactose-restricted diet for life.

9. **Glycogen storage disease (GSD):** For more information see GeneReviews at <http://www.ncbi.nlm.nih.gov/books/NBK1312/> and <http://www.ncbi.nlm.nih.gov/books/NBK26372/>

a. Epidemiology: Autosomal recessive

(1) GSD type I: 1/100,000; GSD1a most common in persons of European descent

(2) GSD type III: 1/100,000

b. Presentation:

(1) GSD type I: Patients have hepatomegaly and renomegaly. They can present with severe hypoglycemia in the neonatal period, but more commonly present at age 3–4 months with hepatomegaly, lactic acidosis, hyperuricemia, hypoglycemia, and hyperlipidemia. They have doll-like facies and xanthomas. Progression of disease includes long-term growth retardation, short stature, osteoporosis, delayed puberty, hepatic adenomas, polycystic ovaries, renal disease, and pancreatitis. Unreated GSD1b is associated with recurrent bacterial infections and mucosal ulcers secondary to impaired neutrophil and monocyte function, along with chronic neutropenia.

(2) GSD type III: Patients have liver and muscle involvement. In infancy and early childhood, they present with ketotic hypoglycemia, hepatomegaly, hyperlipidemia, and elevated hepatic transaminases. GSD3a is associated with hypertrophic cardiomyopathy and skeletal myopathy in the third to fourth decade.

c. Diagnosis:

(1) GSD type I: Blood glucose, lactate, uric acid, triglycerides, lipids, molecular genetic testing

(2) GSD type III: Ketotic hypoglycemia with fasting, transaminases, CK, molecular testing

d. Acute management: Prevent hypoglycemia, treat with dextrose-containing fluids.

e. Chronic management:

(1) GSD type I: Prevent hypoglycemia and may have to provide cornstarch or newly available Glycosade after consulting a geneticist.

Allopurinol to prevent gout. Lipid-lowering medications. Citrate supplementation to help prevent nephrolithiasis, nephrocalcinosis. Angiotensin-converting enzyme (ACE) inhibitors to treat microalbuminuria. Kidney transplant for end-stage renal disease. G-CSF for recurrent infections in GSD1b.

- (2) GSD type III: High-protein diet and frequent feedings (Q3–4 hr) in infancy. Cornstarch or Glycosade to prevent hypoglycemia overnight.

#### F. Hypotonia<sup>11,12</sup>

1. **Definition:** Reduced resistance to passive range of motion in joints, characterized by an impaired ability to sustain postural control and movement against gravity.
2. **Central:** Depressed level of consciousness, predominantly axial weakness, normal strength with hypotonia, abnormalities of brain function, dysmorphic features, fisting of the hands, scissoring on vertical suspension, and other congenital malformations (Fig. 13-4A).
3. **Peripheral:** Alert, responds appropriately to surroundings, normal sleep/wake cycles, profound weakness, absent reflexes, feeding difficulties, decreased and/or lack of antigravity movement (see Fig. 13-4B).
4. **Combined hypotonia:** See Fig. 13-5

### III. DYSMORPHOLOGY<sup>1,2,13-15</sup>

#### A. History

Pregnancy history, type of conception (natural vs. artificial reproductive technologies), perinatal history, developmental milestones, three-generation pedigree

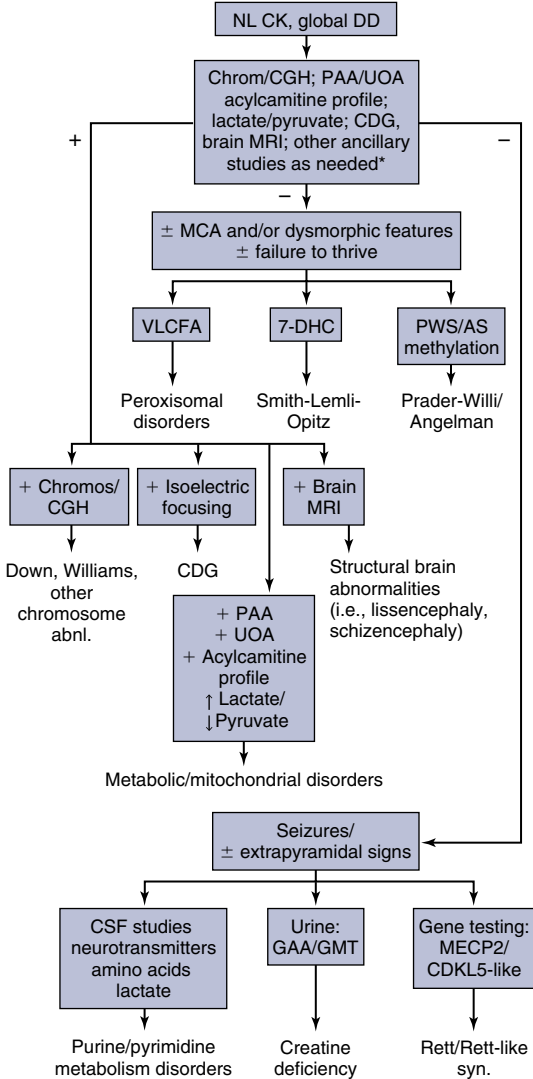
#### B. Physical Examination<sup>13</sup>

1. **Major anomalies:** Create significant medical problems for the patient and may require specific surgical or medical management. Includes structural brain abnormalities, intellectual disability or developmental delays, failure to thrive, cleft lip and/or palate, congenital heart defects, skeletal dysplasia, severe limb abnormalities.
2. **Minor anomalies:** Features that vary in comparison to the normal population, with little serious medical or surgical consequences. Includes abnormally shaped ears or eyes, inverted nipples, birthmarks, abnormal structures of the hands and feet, abnormal skin folds or creases (e.g., single palmar crease).

#### C. Workup

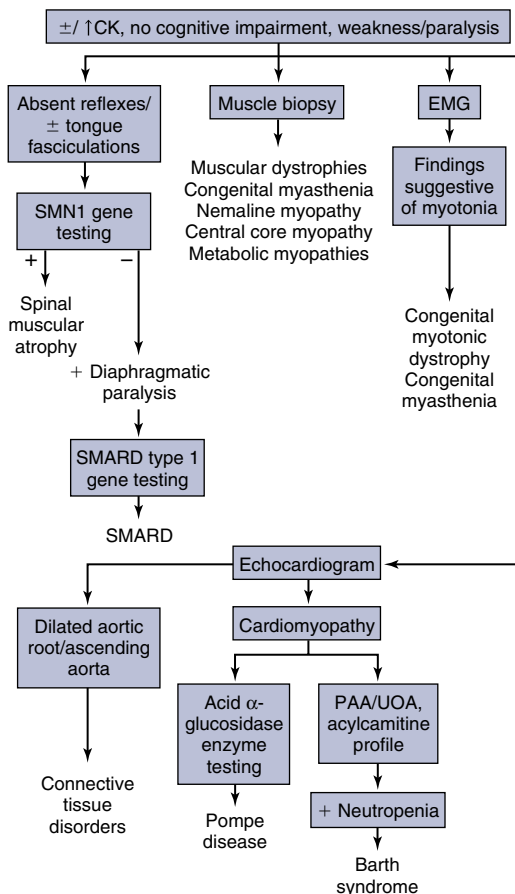
1. **Imaging:**
  - a. Abdominal ultrasound, echocardiogram, brain imaging (head ultrasound or magnetic resonance imaging [MRI])
  - b. Genetic skeletal survey for patients with apparent short bones, short stature, visible external anomalies (asymmetry, proximal thumbs, skin dimpling)





**A (Central Hypotonia)**

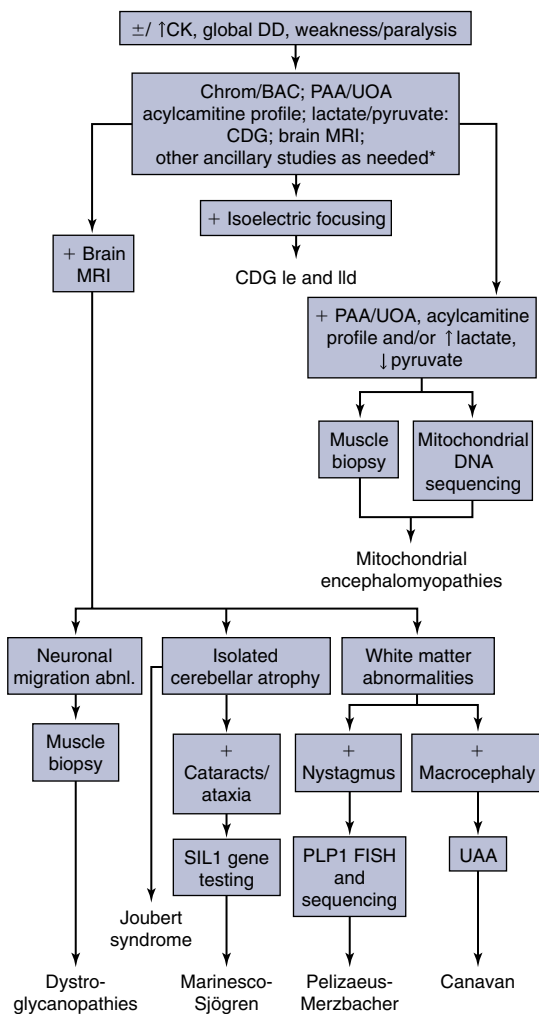
**FIGURE 13-4, cont'd**



## B (Peripheral Hypotonia)

**FIGURE 13-4**

Hypotonia. CDKL5, cyclin-dependent kinase-like 5; CK, creatine kinase; CPT II, carnitine palmitoyltransferase II; CSF, cerebrospinal fluid; DD, developmental delay; 7-DHC, 7-dehydrocholesterol; EMG, electromyography; GAA, guanidinoacetate; GMT, guanidinoacetate-N-methyltransferase; MCA, multiple congenital anomalies; MECP2, methyl CpG binding protein 2; NL CK, normal creatine kinase; PAA, plasma amino acids; PWS/AS, Prader-Willi syndrome/Angelman syndrome; SMARD, spinal muscular atrophy with respiratory distress; SMN1, survival of motor neuron 1; UAA, urine amino acids; UOA, urine organic acids; VLCFA, very long-chain fatty acids. (From Lisi E, Cohn R. *Genetic evaluation of the hypotonic pediatric patient: perspective from a hypotonia specialty clinic and review of the literature*. Dev Med Child Neurol. 2011;53:586-599.)

**FIGURE 13-5**

Combined hypotonia. FISH, fluorescence in situ hybridization; PLP1, proteolipid protein 1. (From Lisi E, Cohn R. Genetic evaluation of the hypotonic pediatric patient: perspective from a hypotonia specialty clinic and review of the literature. *Dev Med Child Neurol*. 2011;53:586-599.)

2. **Ophthalmologic examination**
3. **Hearing evaluation**
4. **Chromosome microarray:** Indicated when one major and two minor malformations are present; detects changes in copy number and genotype. This is first-line testing for chromosomal anomalies replacing the karyotype, except when specifically indicated (see below). This test may be done by single nucleotide polymorphism (SNP) array (which will also detect low-level mosaicism and consanguinity) or oligoarray. Both assays are equally sensitive at detecting copy number variation.
5. **Specific gene testing:** See [www.genetests.org](http://www.genetests.org) for reference.
6. **Whole-exome sequencing:** Consult a geneticist. This tests yields complex results well beyond the diagnosis and requires extensive pretest and posttest counseling.
7. **Karyotype:** Very rarely indicated anymore; indicated in suspected aneuploidy (e.g., trisomy 13, 18, 21, or monosomy X) and when assessing frequent miscarriages (to look for balanced translocation). Otherwise, first-line testing for chromosome abnormalities is a microarray.
8. **Fluorescence in situ hybridization (FISH):** Only rarely indicated.

#### D. Specific Syndromes

This section is not comprehensive; it covers a few common genetic syndromes. More complete information can be found in the following references: Jones<sup>14</sup>, Hall and colleagues<sup>13</sup>, <http://omim.org>, [www.genereviews.org](http://www.genereviews.org):

1. **Trisomy 21**<sup>16</sup>:
  - a. Epidemiology: Occurs in 1/700–1/1000 newborns (risk increases with advanced maternal age).
  - b. Most commonly due to maternal nondisjunction in 95%; few cases due to translocation (3%–4%).
  - c. Presentation: Hypotonia, small brachycephalic head, epicanthic folds, flat nasal bridge, upward-slanting palpebral fissures, Brushfield spots, small mouth, small ears, excessive skin at the nape of the neck, single transverse palmar (simian) crease, short fifth finger with clinodactyly, wide gap between the first and second toes, intellectual disability with a range from mild to severe, increased risk of congenital heart defects (50%), leukemia (<1%), hearing loss (75%), otitis media (50%–70%), Hirschsprung disease (<1%), gastrointestinal atresias (12%), eye disease (60%) including cataracts (15%) and severe refractive errors (50%), acquired hip dislocation (6%), obstructive sleep apnea (50%–75%), and thyroid disease (15%).
  - d. Diagnostic evaluation: First trimester screening with follow-up testing if increased risk; follow-up testing available includes noninvasive prenatal diagnosis with fetal circulating DNA in maternal serum; definitive results available through karyotype analysis at birth or prenatally by amniocentesis or chorionic villi sampling (CVS).
  - e. Health supervision: Guideline available at <http://pediatrics.aappublications.org/content/107/2/442.full.html>:

- (1) Neonatal: Ophthalmologic evaluation for cataracts, hearing screen, echocardiogram, obtain complete blood count due to increased risk for leukemia vs. transient myeloproliferative disorder, consider ear-nose-throat (ENT) evaluation for any airway concerns, check thyroid studies or confirm normal on newborn screen (1% congenital hypothyroidism), early intervention services.
- (2) Infancy: Risk of serous otitis media 50%–70%, may need referral to ENT if any concern for hearing loss, behavioral audiogram in all children at 1 year, evaluate vision at each visit, refer at 6 months for pediatric ophthalmology visit, thyroid studies at 6 and 12 months and then annually, early intervention services.
- (3) Early childhood: Consider referral to ENT and audiology if concern for hearing loss, subjective evaluation of vision at each visit, referral to pediatric ophthalmology every 2 years, cervical spine roentgenogram at age 3 to 5 years to look for atlantoaxial instability or subluxation, thyroid screening annually, monitor for signs of obstructive sleep apnea.
- (4) Late childhood: Audiologic and ophthalmologic exams annually, thyroid studies annually.
- (5) Adolescence: Perform CBC and thyroid function tests, annual audiologic and ophthalmologic examinations.

## 2. **Trisomy 18**<sup>14</sup>:

- a. Epidemiology: 1/5000 newborns (increased risk with advanced maternal age).
- b. Most commonly due to maternal nondisjunction.
- c. Features: Intrauterine growth restriction and polyhydramnios, small for gestational age at birth, clenched hands with overlapping fingers, hypoplastic nails, short sternum, prominent occiput, low-set and structurally abnormal ears, micrognathia, rocker-bottom feet, congenital heart disease, cystic and horseshoe kidneys, failure to thrive, seizures, hypertonia, significant developmental and cognitive impairments.
- d. Diagnosis: First trimester screening with follow-up testing if increased risk; follow-up testing available includes noninvasive prenatal diagnosis with fetal circulating DNA in maternal serum; definitive results available through karyotype analysis at birth or prenatally by amniocentesis or chorionic villi sampling (CVS); approximately 90% will have abnormalities on ultrasound.
- e. Previously thought to be invariably lethal in the neonatal period, now approximately 5%–10% make it to their first birthday.

## 3. **Trisomy 13**<sup>14</sup>:

- a. Epidemiology: 1/5000 newborns (increased risk with advanced maternal age).
- b. Features: Defects of forebrain development (holoprosencephaly), severe developmental disability, low-set malformed ears, cleft lip and palate, microphthalmia, scalp defects, aplasia cutis congenita, polydactyly (most frequently of the postaxial type), narrow hyperconvex nails, apneic spells, cryptorchidism, congenital heart defects.

- c. Diagnosis: First-trimester screening with follow-up testing if increased risk. Available follow-up testing includes noninvasive prenatal diagnosis with fetal circulating DNA in maternal serum; definitive results available through karyotype analysis at birth or prenatally by amniocentesis or chorionic villi sampling (CVS); about 90% will have abnormalities on ultrasound.
  - d. Roughly 5% of pregnancies with trisomy 13 survive to birth, and only 5% of those survive the first 6 months of life.
4. **Turner syndrome (45,X)**<sup>14,17</sup>:
- a. Epidemiology: 1/2000–5000 newborns (99% spontaneously abort).
  - b. Features: Slight intrauterine growth restriction, slow growth during infancy and childhood, gonadal dysgenesis and lack of a pubertal growth spurt. Intelligence is usually normal, but patients are at risk for cognitive, behavioral, and social impairments. Other features are lymphedema, micrognathia, dental crowding, deep-set and hyperconvex nails, broad chest with hypoplastic or inverted nipples, tibial exostosis, hearing loss, renal abnormalities, webbed neck, hypertension, congenital heart disease (most commonly bicuspid aortic valve and coarctation of the aorta), and hypothyroidism.
  - c. Diagnosis: Karyotype
  - d. Health supervision: Guidelines available at <http://pediatrics.aappublications.org/content/111/3/692.full.html>:
    - (1) Endocrine: Growth hormone usually initiated when height < 5th percentile (refer early to pediatric endocrinology), monitor for obesity and glucose intolerance, monitor for thyroid dysfunction.
    - (2) Cardiology: Baseline echocardiogram, close cardiac follow-up to monitor for aortic dilatation, monitor for hypertension and manage aggressively.
    - (3) HEENT: Hearing examination and audiology referral, monitor for strabismus.
    - (4) Renal: Evaluate for renal abnormalities (most commonly a horseshoe kidney).
    - (5) Orthopedic: Hip examinations in infancy because of increased risk of congenital developmental hip dysplasia; evaluate for development of scoliosis.
    - (6) Provide psychosocial support.
5. **Connective tissue diseases**<sup>14,18,19</sup>:
- a. Examples: Marfan, Loays-Dietz, familial thoracic aortic aneurysm disease, bicuspid aortic valve and aneurysm syndromes, Ehlers-Danlos, Sphrintzen-Goldberg, cutis laxa syndromes, arterial tortuosity syndrome, Stickler syndrome (description of each of these is beyond the scope of this chapter).
  - b. Marfan: Prevalence 1/5000–10,000; autosomal dominant. Diagnostic criteria incorporate information from family history, medical history, physical examination, slit lamp examination, echocardiography.

## (1) Features:

- (a) Myopia, displacement of the lens from the center of the pupil (60%), bone overgrowth and joint laxity, extremities disproportionately long for size of trunk, pectus carinatum or excavatum, scoliosis, dilatation of the aorta at level of sinuses of Valsalva, predisposition to aortic tear and rupture, mitral valve prolapsed, enlargement of proximal pulmonary artery, pneumothorax
- (b) Physical examination: Scoring of systemic features based on evaluation of the literature available at <http://www.marfan.org/marfan/4470/Diagnostic-Criteria----Scoring-of-Systemic-Features/>

## (2) Diagnosis confirmed by molecular genetic testing of fibrillin-1 gene (FBN1).

(3) Surveillance: Annual ophthalmologic examination; annual echocardiography unless aortic root diameter exceeds  $\approx 4.5$  cm in adults (rates of aortic dilation exceed  $\approx 0.5$  cm/yr) and significant aortic regurgitation is present, then valve-sparing surgery to replace the aortic root; intermittent surveillance of the entire aorta with computed tomography (CT) or magnetic resonance angiography (MRA) scans beginning in young adulthood. Avoid contact sports, competitive sports, isometric exercise, and overstimulation of the cardiovascular system.(4) Treatment with  $\beta$ -blocker (atenolol) is current standard of care, but a large-scale trial is underway to see whether angiotensin-II type 1 receptor blocker (losartan) may be more effective.6. **Neurofibromatosis type I (NF1)**<sup>14,20</sup>:

## a. Epidemiology: 1/4000; autosomal dominant

## b. Diagnosis:

- (1) Two or more of the following: Six or more café au lait macules over 5 mm in greatest diameter in prepubertal individuals and over 15 mm greatest diameter in postpubertal individuals, two or more neurofibromas of any type or one plexiform neurofibroma, freckling in the axillary or inguinal regions, optic glioma, two or more Lisch nodules, a distinctive osseous lesion (e.g., sphenoid dysplasia, tibial pseudarthrosis), a first-degree relative (parent, sibling, offspring) with NF1 as defined by the above criteria
- (2) Other features: Short stature, macrocephaly, progressive scoliosis
- (3) Diagnostic evaluation: Molecular confirmation by NF1 gene testing

## c. Surveillance: Annual genetics examination, annual ophthalmologic examination, developmental assessment of children, regular blood pressure monitoring, MRI for follow-up of clinically symptomatic tumors

7. **22q11 syndrome (velocardiofacial syndrome [VCFS], DiGeorge syndrome)**<sup>15</sup>:

## a. Epidemiology: 1/4000–6000; autosomal dominant.

## b. Features: Congenital heart disease (tetralogy of Fallot, interrupted aortic arch, ventricular septal defect, and truncus arteriosus most common), palatal abnormalities (velopharyngeal incompetence [VPI], cleft palate),

characteristic facial features, learning difficulties, immune deficiency (70%), hypocalcemia (50%), significant feeding problems (30%), renal anomalies (37%), hearing loss (both conductive and sensorineural), laryngotracheoesophageal anomalies, growth hormone deficiency, autoimmune disorders, seizures (without hypocalcemia), and skeletal abnormalities.

- c. Diagnostic evaluation: SNP array is the gold standard; FISH is no longer recommended as first line. Assessments should include serum calcium, absolute lymphocyte count, B- and T-cell subsets, renal ultrasound, chest x-ray, cardiac examination, and echocardiogram.
- 8. **Fragile X syndrome**<sup>21</sup>:
  - a. Epidemiology: 1/4000 males and 1/8000 females; X-linked
  - b. Features:
    - (1) Male: Mild to moderate intellectual disability, cluttered speech, autism, macrocephaly, large ears, prognathism, postpubertal macroorchidism, tall stature, seizures, tremor, ataxia
    - (2) Female: A third are intellectually disabled; premature ovarian failure, tremor, ataxia
  - c. Diagnostic evaluation: Molecular genetic testing of the FMR1 gene; caused by expansion of the CGG nucleotide repeat in the FMR1 gene

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# Chapter 14

## Hematology

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### I. ANEMIA

#### A. General Evaluation

Anemia is defined as a reduction in hemoglobin (Hb) two standard deviations below the mean, based on age-specific norms (Table 14-1 and Fig. 14-1). Evaluation should include:

1. **Complete history**, including nutrition, menstruation, ethnicity, fatigue, pica, medication exposure, growth and development, blood loss, hyperbilirubinemia and family history of anemia, splenectomy, or cholecystectomy.
2. **Physical examination**, including evaluation of pallor, tachycardia, cardiac murmur, jaundice, hepatosplenomegaly, glossitis, tachypnea, koilonychia, angular cheilitis or signs of systemic illness.
3. **Initial laboratory tests** including complete blood cell count (CBC) with red blood cell (RBC) indices (mean corpuscular volume [MCV], mean corpuscular hemoglobin [MCH], red cell distribution width [RDW]), reticulocyte count, stool for occult blood, urinalysis, and serum bilirubin. Complete evaluation always includes a peripheral blood smear.

#### B. Diagnosis

Anemias may be categorized as macrocytic, microcytic, or normocytic. Table 14-2 gives an approach to diagnosis based on RBC production as measured by reticulocyte count and cell size. Note that normal ranges for Hb and MCV are age dependent.

#### C. Evaluation of Specific Causes of Anemia

1. **Iron-deficiency anemia:** Hypochromic/microcytic anemia with a low reticulocyte count and an elevated RDW.
  - a. Serum ferritin reflects total body iron stores after age 6 months and is the first value to fall in iron deficiency; may be falsely elevated with inflammation or infection.
  - b. Other indicators: Low serum iron, elevated total iron-binding capacity (TIBC), low mean corpuscular hemoglobin concentration (MCHC), elevated transferrin receptor level, and low reticulocyte Hb content.
  - c. Iron therapy should result in an increased reticulocyte count in 2–3 days and an increase in hematocrit (HCT) after 1–4 weeks of therapy. Iron stores are generally repleted after 3 months of therapy.
  - d. Mentzer index (MCV/RBC): Index >13.5 suggests iron deficiency; expect elevated RDW. Mentzer index <11.5 suggests thalassemia minor; expect low/normal RDW.

TABLE 14-1

## AGE-SPECIFIC BLOOD CELL INDICES

Age	Hb (g/dL)*	HCT (%)*	MCV (fL)*	MCHC (g/dL RBC)*	Reticulocytes	WBCs ( $\times 10^3/\text{mL}$ )†	Platelets ( $10^3/\text{mL}$ )‡
26–30 wk gestation‡	13.4 (11)	41.5 (34.9)	118.2 (106.7)	37.9 (30.6)	—	4.4 (2.7)	254 (180–327)
28 wk	14.5	45	120	31.0	(5–10)	—	275
32 wk	15.0	47	118	32.0	(3–10)	—	290
Term§ (cord)	16.5 (13.5)	51 (42)	108 (98)	33.0 (30.0)	(3–7)	18.1 (9–30)	290
1–3 day	18.5 (14.5)	56 (45)	108 (95)	33.0 (29.0)	(1.8–4.6)	18.9 (9.4–34)	192
2 wk	16.6 (13.4)	53 (41)	105 (88)	31.4 (28.1)	—	11.4 (5–20)	252
1 mo	13.9 (10.7)	44 (33)	101 (91)	31.8 (28.1)	(0.1–1.7)	10.8 (4–19.5)	—
2 mo	11.2 (9.4)	35 (28)	95 (84)	31.8 (28.3)	—	—	—
6 mo	12.6 (11.1)	36 (31)	76 (68)	35.0 (32.7)	(0.7–2.3)	11.9 (6–17.5)	—
6 mo–2 yr	12.0 (10.5)	36 (33)	78 (70)	33.0 (30.0)	—	10.6 (6–17)	(150–350)
2–6 yr	12.5 (11.5)	37 (34)	81 (75)	34.0 (31.0)	(0.5–1.0)	8.5 (5–15.5)	(150–350)
6–12 yr	13.5 (11.5)	40 (35)	86 (77)	34.0 (31.0)	(0.5–1.0)	8.1 (4.5–13.5)	(150–350)
<b>12–18 YR</b>							
Male	14.5 (13)	43 (36)	88 (78)	34.0 (31.0)	(0.5–1.0)	7.8 (4.5–13.5)	(150–350)
Female	14.0 (12)	41 (37)	90 (78)	34.0 (31.0)	(0.5–1.0)	7.8 (4.5–13.5)	(150–350)
<b>ADULT</b>							
Male	15.5 (13.5)	47 (41)	90 (80)	34.0 (31.0)	(0.8–2.5)	7.4 (4.5–11)	(150–350)
Female	14.0 (12)	41 (36)	90 (80)	34.0 (31.0)	(0.8–4.1)	7.4 (4.5–11)	(150–350)

\*Data are mean ( $\pm$  2 SD).†Data are mean ( $\pm$  2 SD).

‡Values are from fetal samplings.

§1 mo, capillary hemoglobin exceeds venous: 1 hr: 3.6-g difference; 5 day: 2.2-g difference; 3 wk: 1.1-g difference.

||Mean (95% confidence limits).

Hb, Hemoglobin; HCT, hematocrit; MCHC, mean cell hemoglobin concentration; MCV, mean corpuscular volume; RBC, red blood cell; WBC, white blood cell.

Data from Forestier F, Dattos F, Galacteros F, et al. Hematologic values of 163 normal fetuses between 18 and 30 weeks of gestation. *Pediatr Res*. 1986;20:342; Oski FA, Naiman JL. *Hematological Problems in the Newborn Infant*. Philadelphia: WB Saunders; 1982; Nathan D, Oski FA. *Hematology of Infancy and Childhood*. Philadelphia: WB Saunders; 1998; Matoth Y, Zaizor K, Varsano I, et al. Postnatal changes in some red cell parameters. *Acta Paediatr Scand*. 1971;60:317; and Wintrobe MM. *Clinical Hematology*. Baltimore: Williams & Wilkins; 1999.

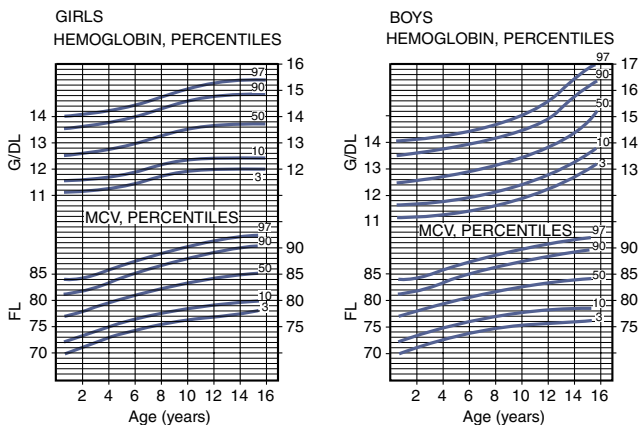


FIGURE 14-1

Hemoglobin and mean corpuscular volume (MCV) by age and gender. (Data from Dallman PR, Siimes MA. Percentile curves for hemoglobin and red cell volume in infancy and childhood. *J Pediatr.* 1979;94:26.)

2. **Hemolytic anemia:** Rapid RBC turnover. Etiologies: Congenital membranopathies, hemoglobinopathies, enzymopathies, metabolic defects, and immune-mediated destruction. Useful studies include:
  - a. Reticulocyte count: Usually elevated; indicates increased production of RBCs to compensate for increased destruction. Corrected reticulocyte count (CRC) accounts for differences in HCT and is an indicator of erythropoietic activity.  $\text{CRC} > 1.5$  suggests increased RBC production secondary to hemolysis or blood loss.
 
$$\text{CRC} = \% \text{ Reticulocytes} \times \text{Patient HCT} / \text{Normal HCT}$$
  - b. Plasma aspartate aminotransferase (AST) and lactate dehydrogenase (LDH): Increased from release of intracellular enzymes. Serum LDH levels are significantly elevated in intravascular hemolysis and mildly elevated in extravascular hemolysis.
  - c. Haptoglobin: Binds free Hb; decreased with intravascular and extravascular hemolysis. Can also be decreased in patients with liver dysfunction secondary to decreased hepatic synthesis and in neonates.
  - d. Direct Coombs test: Tests for presence of antibody or complement on patient RBCs. May be falsely negative if affected cells have already been destroyed or antibody titer is low.
  - e. Indirect Coombs test: Tests for free autoantibody in patient's serum after RBC antibody binding sites are saturated. Positive indirect test with negative direct test is typical of alloimmune sensitization (e.g., transfusion reaction).

**TABLE 14-2**  
**CLASSIFICATION OF ANEMIA**

Reticulocyte Count	Microcytic Anemia	Normocytic Anemia	Macrocytic Anemia
Low	Iron deficiency Lead poisoning Chronic disease Aluminum toxicity Copper deficiency Protein malnutrition	Chronic disease RBC aplasia (TEC, infection, drug induced) Malignancy Juvenile rheumatoid arthritis Endocrinopathies Renal failure	Folate deficiency Vitamin B <sub>12</sub> deficiency Aplastic anemia Congenital bone marrow dysfunction (Diamond-Blackfan or Fanconi syndromes) Drug-induced Trisomy 21 Hypothyroidism
Normal	Thalassemia trait Sideroblastic anemia	Acute bleeding Hypersplenism Dyserythropoietic anemia II	—
High	Thalassemia syndromes Hemoglobin C disorders	Antibody-mediated hemolysis Hypersplenism Microangiopathy (HUS, TTP, DIC, Kasabach-Merritt) Membranopathies (spherocytosis, elliptocytosis) Enzyme disorders (G6PD, pyruvate kinase) Hemoglobinopathies	Dyserythropoietic anemia I, III Active hemolysis

DIC, Disseminated intravascular coagulation; G6PD, glucose-6-phosphate dehydrogenase; HUS, hemolytic-uremic syndrome; RBC, red blood cell; TEC, transient erythroblastopenia of childhood; TTP, thrombotic thrombocytopenic purpura.

Data from Nathan D, Oski FA. *Hematology of Infancy and Childhood*, 6th ed. Philadelphia: WB Saunders, 2003.

- f. Osmotic fragility test: Useful in diagnosis of hereditary spherocytosis. Can also be positive in ABO incompatibility, autoimmune hemolytic anemia, or anytime spherocytes are present.
- g. Glucose-6-phosphate dehydrogenase (G6PD) assay: Quantitative test to diagnose G6PD deficiency, an X-linked disorder affecting 10%–14% of African American males. May be normal immediately after a hemolytic episode because older, more enzyme-deficient cells have been lysed. For a comprehensive list of oxidizing drugs, go to: <http://g6pddeficiency.org/index.php?cmd=contraindicated>.

- h. Heinz body preparation: detects precipitated Hb within RBCs; present in unstable hemoglobinopathies and enzymopathies during oxidative stress (e.g., G6PD deficiency).
3. **Red cell aplasia:** variable cell size, low reticulocyte count, variable platelet and white blood cell (WBC) counts. Bone marrow aspiration evaluates RBC precursors in the marrow to look for marrow dysfunction, neoplasm, or specific signs of infection.
- a. Acquired aplasias:
  - (1) Infectious causes: parvovirus in children with rapid RBC turnover (infects RBC precursors), Epstein-Barr virus (EBV), cytomegalovirus (CMV), human herpesvirus type 6, or human immunodeficiency virus (HIV).
  - (2) Transient erythroblastopenia of childhood (TEC): Occurs from age 6 months to 4 years, with >80% of cases presenting after age 1 year with a normal or slightly low MCV and low reticulocyte count. Spontaneous recovery usually occurs within 4–8 weeks.
  - (3) Exposures include radiation and various drugs and chemicals.
- b. Congenital aplasias: Typically macrocytic anemias
  - (1) Fanconi anemia: Autosomal recessive disorder, usually presents before 10 years of age; may present with pancytopenia. Patients may have thumb abnormalities, renal anomalies, microcephaly, or short stature. Chromosomal fragility studies can be diagnostic.
  - (2) Diamond-Blackfan anemia: Autosomal recessive pure RBC aplasia; presents in the first year of life. Associated with congenital anomalies in 30%–47%<sup>12</sup> of cases, including triphalangeal thumb, short stature, and cleft lip.
- c. Aplastic anemia: Idiopathic bone marrow failure, usually macrocytic.
4. **Physiologic anemia of infancy (physiologic nadir):** Decrease in Hb until oxygen needs exceed oxygen delivery, usually at Hb of 9–11 mg/dL. Normally occurs at age 8–12 weeks for full-term infants and age 3–6 weeks for preterm infants.
5. **Anemia of chronic inflammation:** usually normocytic with normal to low reticulocyte count. Iron studies reveal low iron, TIBC, and transferrin and elevated ferritin.

## II. HEMOGLOBINOPATHIES

### A. Hemoglobin Electrophoresis

Involves separation of Hb variants based on molecular charge and size. All positive sickle preparations and solubility tests for sickle Hb (e.g., Sickledex) should be confirmed with electrophoresis or isoelectric focusing (component of mandatory newborn screening in many states). [Table 14-3](#) outlines neonatal Hb electrophoresis patterns.

### B. Sickle Cell Anemia

Caused by a genetic defect in  $\beta$ -globin; 8% of African Americans are carriers; 1 in 500 African Americans have sickle cell anemia.

**TABLE 14-3**  
**NEONATAL HEMOGLOBIN (Hb) ELECTROPHORESIS PATTERNS\***

FA	Fetal Hb and adult normal Hb; the normal newborn pattern
FAV	Indicates presence of both HbF and HbA, but an anomalous band (V) is present that does not appear to be any of the common Hb variants.
FAS	Indicates fetal Hb, adult normal HbA, and HbS, consistent with benign sickle cell trait
FS	Fetal and sickle HbS without detectable adult normal HbA. Consistent with clinically significant homozygous sickle Hb genotype (S/S) or sickle $\beta$ -thalassemia, with manifestations of sickle cell anemia during childhood.
FC†	Designates presence of HbC without adult normal HbA. Consistent with clinically significant homozygous HbC genotype (C/C), resulting in a mild hematologic disorder presenting during childhood.
FSC	HbS and HbC present. This heterozygous condition could lead to manifestations of sickle cell disease during childhood.
FAC	HbC and adult normal HbA present, consistent with benign HbC trait
FSA	Heterozygous HbS/ $\beta$ -thalassemia, a clinically significant sickling disorder
F†	Fetal HbF is present without adult normal HbA. May indicate delayed appearance of HbA but is also consistent with homozygous $\beta$ -thalassemia major or homozygous hereditary persistence of fetal HbF.
FV†	Fetal HbF and an anomalous Hb variant (V) are present.
AF	May indicate prior blood transfusion. Submit another filter paper blood specimen when infant is 4 mo of age, at which time the transfused blood cells should have been cleared.

\*Hemoglobin variants are reported in order of decreasing abundance; for example, FA indicates more fetal than adult hemoglobin.

†Repeat blood specimen should be submitted to confirm original interpretation.

**NOTE:** HbA:  $\alpha_2\beta_2$ ; HbF:  $\alpha_2\gamma_2$ ; HbA<sub>2</sub>:  $\alpha_2\delta_2$ .

1. **Diagnosis:** Often made on newborn screen with Hb electrophoresis. The sickle preparation and Sickledex are rapid tests that are positive in all sickle hemoglobinopathies. False-negative test results may be seen in neonates and other patients with a high percentage of fetal Hb.
2. **Complications** (Table 14-4): A hematologist should be consulted.
3. **Health maintenance**<sup>1,2</sup>: Ongoing consultation and clinical involvement with a pediatric hematologist and/or sickle cell program are essential (Table 14-5).
4. **Hemoglobin electrophoresis (outside neonatal period):** hemoglobin SF, SCF, SAF—other Hb combinations may sickle.

**C. Thalassemias**

Defects in  $\alpha$ - or  $\beta$ -globin production. The predominant adult hemoglobin is HbA ( $\alpha_2\beta_2$ ), a tetramer composed of two  $\alpha$  and two  $\beta$  chains. The  $\alpha$ -Globin production is dependent on four genes, and  $\beta$ -globin production is dependent on two genes. Imbalance in production of globin chains leads to precipitation of excess chains, causing ineffective erythropoiesis and shortened survival of mature RBCs.

**1.  $\alpha$ -Thalassemias:**

- a. Silent carriers ( $\alpha\text{--}/\alpha\alpha$ ): not anemic, childhood and adult hemoglobin electrophoresis usually normal.

TABLE 14-4

## SICKLE CELL DISEASE COMPLICATIONS

Complication	Evaluation	Treatment
<b>Fever (<math>T \geq 38.5^{\circ}\text{C}</math>)</b>	History and physical CBC with differential Reticulocyte count Blood cultures Chest x-ray Other cultures as indicated	IV antibiotics (third-generation cephalosporin, other antibiotics as indicated, especially if penicillin-resistant pneumococcus suspected) Admit if ill appearing, <3 yr of age, concerning lab results, or complications. Some centers use antibiotics with a long half-life and reevaluate in 24 hr as an outpatient.
<b>Vaso-occlusive crisis</b> Children <2 yr, dactylitis Children >2 yr, unifocal or multifocal pain	History and physical CBC with differential Reticulocyte count Type and screen	Oral analgesics as an outpatient, as tolerated IV analgesics and IV fluids if outpatient therapy fails (parenteral narcotics in form of PCA and parenteral NSAIDs, usually in combination) Aggressive early treatment of pain is essential.
<b>Acute chest syndrome</b> New pulmonary infiltrate with fever, cough, chest pain, tachypnea, dyspnea, or hypoxia	History and physical CBC with differential Reticulocyte count Blood cultures Chest x-ray Type and screen	Admit $\text{O}_2$ , incentive spirometry, bronchodilators IV antibiotics (third-generation cephalosporin and macrolide) Analgesia, IV fluids Simple transfusion or partial exchange for moderately severe illness; double the packed cell volume exchange transfusion for severe or rapidly progressing illness. High-dose dexamethasone controversial (risk of readmission for pain or other SCD-related issues) <sup>7</sup>
<b>Splenic sequestration</b> Acutely enlarged spleen and Hb level $\geq 2$ g/dL below patient's baseline	History and physical CBC Reticulocyte count Type and hold	Serial abdominal exams IV fluids and fluid resuscitation as necessary RBC transfusion or, in severe cases, exchange transfusion for cardiovascular compromise and Hb <4.5 g/dL. (Autotransfusion may occur with recovery, leading to increased Hb and CHF. Transfuse cautiously.)

*Continued*



**TABLE 14-4**

**SICKLE CELL DISEASE COMPLICATIONS (Continued)**

Complication	Evaluation	Treatment
<b>Aplastic crisis</b>	History and physical	Admit
Acute illness with Hb below patient's baseline and low reticulocyte count	CBC with differential Reticulocyte count Type and screen	IV fluids PRBCs for symptomatic anemia Isolation to protect susceptible individuals and women of childbearing age until parvovirus excluded
May follow viral illnesses, especially parvovirus B19	Parvovirus serology and polymerase chain reaction	

**Other complications**

Priapism, CVA, TIA, gallbladder disease, avascular necrosis, hyphema\*

\*Hyphema in a patient with sickle cell trait is an ophthalmologic emergency

**NOTE:** CVA requires emergency transfusion guided by a hematologist and a neurologist experienced with sickle cell disease. Exchange transfusion preferable to simple transfusion if possible.<sup>8</sup>

Abbreviations: CBC, Complete blood cell count; CHF, congestive heart failure; CVA, cerebrovascular accident; Hb, hemoglobin; IV, intravenous; NSAIDs, nonsteroidal anti-inflammatory drugs; PCA, patient-controlled analgesia; PRBCs, packed red blood cells; RBC, red blood cells; SCD, sickle cell disease; T, temperature; TIA, transient ischemic attack.

**TABLE 14-5**

**SICKLE CELL DISEASE HEALTH MAINTENANCE**

IMMUNIZATIONS	Maintenance
Pneumococcal vaccine	Vaccinate with 13-valent conjugate vaccine as per routine childhood schedule, 23-valent polysaccharide vaccine at age 2, booster at age 5.
Meningococcal vaccine	Give at age 2 and every 5 yr thereafter.
Influenza vaccine	Vaccinate yearly beginning at age 6 mo.
<b>MEDICATIONS</b>	
PCN	Begin as soon as SCD diagnosis made (125 mg BID; increase dose to 250 mg BID at age 3*).
Folic acid	Consider supplementation, start by age 1.
Hydroxyurea	Consider with frequent crises or in severe disease. <sup>†</sup>
<b>IMAGING</b>	
Transcranial Doppler (TCD)	Perform annually from ages 2 to 16 to evaluate for increased risk of cerebrovascular accident (CVA).
<b>OTHER</b>	
Ophthalmology	Perform annually from age 10 to evaluate for sickle retinopathy.
Growth and development, school/social issues, counseling regarding fevers	Review closely at all visits.

\*Prophylaxis may be discontinued by age 5 if patient has had no prior severe pneumococcal infections or splenectomy and has documented pneumococcal vaccinations, including second 23-valent vaccination. Practice patterns vary. Some continue penicillin indefinitely.

<sup>†</sup>Increases levels of fetal Hb and decreases HbS polymerization in cells. Has been shown to significantly decrease episodes of vaso-occlusive crises, dactylitis, acute chest syndrome, number of transfusions, and hospitalizations.<sup>9,13</sup> May decrease mortality in adults.

PCN, Penicillin; SCD, sickle cell disease.

- b.  $\alpha$ -Thalassemia trait ( $\alpha\alpha/\alpha-$ ) or ( $\alpha\alpha/\alpha-$ ): Causes mild microcytic anemia, childhood and adult hemoglobin electrophoresis usually normal. Hb Barts can be seen in infancy (e.g., on state newborn screens) in patients with  $\alpha$ -thalassemia trait.
  - c. HbH disease ( $\beta_4$ ) ( $\alpha\alpha/\alpha-$ ): Causes moderately severe anemia.
  - d. Hb Bart/hydrops fetalis ( $---/---$ ): Hb Bart ( $\gamma_4$ ) cannot deliver oxygen; usually fatal.
2.  **$\beta$ -Thalassemia:** Found throughout the Mediterranean, Middle East, India, and Southeast Asia. Ineffective erythropoiesis is more severe in  $\beta$ -thalassemia than  $\alpha$ -thalassemia because excess  $\alpha$  chains are more unstable than  $\beta$  chains. Adult hemoglobin electrophoresis with decreased hemoglobin A, increased hemoglobin A<sub>2</sub>, and increased hemoglobin F.
- a. Thalassemia trait/thalassemia minor ( $\beta/\beta+$ ) or ( $\beta/\beta 0$ ): Usually asymptomatic, with microcytosis out of proportion to anemia, sometimes with erythrocytosis.
  - b. Thalassemia intermedia ( $\beta+/\beta+$ ): Presents at about age 2 years with moderate compensated anemia that may become symptomatic, leading to heart failure, pulmonary hypertension, splenomegaly, and bony expansion, usually in second or third decade of life.
  - c. Thalassemia major/Cooley's anemia ( $\beta 0/\beta 0$ ,  $\beta+/\beta 0$ , or  $\beta+/\beta+$ ): Presence of anemia within first 6 months of life, with hepatosplenomegaly and progressive bone marrow expansion that may lead to frontal bossing, maxillary hyperplasia, and other skeletal deformities. Regular transfusions required to avoid anemia.

### III. NEUTROPENIA

An absolute neutrophil count (ANC)  $<1500/\mu\text{L}$ , although neutrophil counts vary with age (Table 14-6). Severe neutropenia is defined as an ANC  $<500/\mu\text{L}$ . Children with significant neutropenia are at risk for bacterial and fungal infections. Granulocyte colony-stimulating factor may be indicated. Transient neutropenia secondary to viral illness rarely causes significant morbidity. Autoimmune neutropenia is a common cause of neutropenia in children 6 mo–6 yr. Testing for antineutrophil antibodies is indicated in this age group and may obviate the need for more extensive workup. For management of fever and neutropenia in oncology patients, see Chapter 22, Figure 22-1. Box 14-1 lists causes.

### IV. THROMBOCYTOPENIA

#### A. Definition

Platelet count  $<150,000/\mu\text{L}$ . Clinically significant bleeding is unlikely with platelet counts  $>20,000/\mu\text{L}$  in the absence of other complicating factors.

#### B. Causes of Thrombocytopenia

- 1. **Idiopathic thrombocytopenic purpura (ITP):** A diagnosis of exclusion; can be acute or chronic. WBC count, Hb levels, and peripheral blood smear are normal. Many require no therapy, and indications for treatment of patients without significant bleeding are not well established.

**TABLE 14-6**  
**AGE-SPECIFIC LEUKOCYTE DIFFERENTIAL**

Age	Total Leukocytes*	Neutrophils†	%	Lymphocytes	%	Monocytes		Eosinophils	
	Mean (range)	Mean (range)		Mean (range)		Mean	%	Mean	%
Birth	18.1 (9–30)	11 (6–26)	61	5.5 (2–11)	31	1.1	6	0.4	2
12 hr	22.8 (13–38)	15.5 (6–28)	68	5.5 (2–11)	24	1.2	5	0.5	2
24 hr	18.9 (9.4–34)	11.5 (5–21)	61	5.8 (2–11.5)	31	1.1	6	0.5	2
1 wk	12.2 (5–21)	5.5 (1.5–10)	45	5.0 (2–17)	41	1.1	9	0.5	4
2 wk	11.4 (5–20)	4.5 (1–9.5)	40	5.5 (2–17)	48	1.0	9	0.4	3
1 mo	10.8 (5–19.5)	3.8 (1–8.5)	35	6.0 (2.5–16.5)	56	0.7	7	0.3	3
6 mo	11.9 (6–17.5)	3.8 (1–8.5)	32	7.3 (4–13.5)	61	0.6	5	0.3	3
1 yr	11.4 (6–17.5)	3.5 (1.5–8.5)	31	7.0 (4–10.5)	61	0.6	5	0.3	3
2 yr	10.6 (6–17)	3.5 (1.5–8.5)	33	6.3 (3–9.5)	59	0.5	5	0.3	3
4 yr	9.1 (5.5–15.5)	3.8 (1.5–8.5)	42	4.5 (2–8)	50	0.5	5	0.3	3
6 yr	8.5 (5–14.5)	4.3 (1.5–8)	51	3.5 (1.5–7)	42	0.4	5	0.2	3
8 yr	8.3 (4.5–13.5)	4.4 (1.5–8)	53	3.3 (1.5–6.8)	39	0.4	4	0.2	2
10 yr	8.1 (4.5–13.5)	4.4 (1.5–8.5)	54	3.1 (1.5–6.5)	38	0.4	4	0.2	2
16 yr	7.8 (4.5–13.0)	4.4 (1.8–8)	57	2.8 (1.2–5.2)	35	0.4	5	0.2	3
21 yr	7.4 (4.5–11.0)	4.4 (1.8–7.7)	59	2.5 (1–4.8)	34	0.3	4	0.2	3

\*Numbers of leukocytes are  $\times 10^3/\mu\text{L}$ ; ranges are estimates of 95% confidence limits; percents refer to differential counts.

†Neutrophils include band cells at all ages and a small number of metamyelocytes and myelocytes in the first few days of life.

Adapted from Cairo MS, Brauho F. Blood and blood-forming tissues. In: Randolph AM, ed. *Pediatrics*. 21st ed. New York: McGraw-Hill, 2003.

**BOX 14-1**  
**DIFFERENTIAL DIAGNOSIS OF CHILDHOOD NEUTROPENIA**

ACQUIRED	CONGENITAL
Infection	Cyclic neutropenia
Immune-mediated	Severe congenital neutropenia
Chronic benign neutropenia of childhood	(e.g., Kostmann syndrome)
Hypersplenism	Shwachman-Diamond syndrome
Vitamin B <sub>12</sub> , folate, copper deficiency	Fanconi anemia
Drugs or toxic substances	Metabolic disorders (e.g., amino acidopathies, Barth syndrome, glycogen storage disorders)
Aplastic anemia	Osteopetrosis
Malignancies or preleukemic disorders	Neutropenia with pigmentation abnormalities (e.g., Chédiak-Higashi anomaly)
Ionizing radiation	

- a. Treatment options:
  - (1) Intravenous immune globulin (see Formulary for IVIG dosing)
  - (2) Corticosteroids (i.e., prednisone 2 mg/kg/day or up to 30 mg/kg methylprednisolone for up to 3 days)
  - (3) Anti-Rh (D) immune globulin (WinRho). Useful only in Rh-positive nonsplenectomized patients. Should not be used in patients with preexisting hemolysis or renal disease; monitor for signs of intravascular hemolysis after administration. Disseminated intravascular coagulation (DIC) has been reported. See package insert for blackbox warning and monitoring guidelines.
  - (4) Consider rituximab in chronic cases.<sup>3</sup>
  - (5) Splenectomy or chemotherapy may be considered in chronic cases. Platelet transfusions are not generally helpful but necessary in life-threatening bleeding.
2. **Neonatal thrombocytopenia:** May be caused by:
  - a. Decreased production: Results from aplastic disorders, congenital malignancy such as leukemia, and viral infections
  - b. Increased consumption: Usually result of DIC due to infection or asphyxia.
  - c. Immune mediated: Immunoglobulin (Ig)G or complement attach to platelets and cause destruction. Specific causes include preeclampsia, sepsis, maternal ITP, and platelet alloimmunization.
3. **Neonatal alloimmune thrombocytopenia (NAIT):** Transplacental maternal antibodies (usually against PLA-1 antigen/HPA-1a) cause fetal platelet destruction. If severe, a transfusion of maternal platelets will be more effective than random donor platelets in raising infant's platelet count.
- a. Evaluation/diagnosis:
  - (1) Check maternal platelet count and platelet-associated IgG. Mother's platelet count should be normal and platelet-associated IgG usually negative.
  - (2) Absence of maternal PLA-1 antigen/HPA-1a or other specific antigens
  - (3) Study of mother's or infant's plasma with a panel of known minor platelet antigens
  - (4) Mixing study of maternal or neonatal plasma and paternal platelets.
4. **Causes of microangiopathic hemolytic anemia:** DIC, hemolytic-uremic syndrome/thrombotic thrombocytopenic purpura (HUS/TTP)
  - a. HUS/TTP: Characterized by the triad of microangiopathic hemolytic anemia, uremia, and thrombocytopenia. HUS is often triggered by bacterial enteritis, especially caused by *Escherichia coli* O157:H7, although there are a variety of causes. HUS does not typically include coagulation abnormalities like those seen in DIC. Avoid blood products in patients with HUS thought to be secondary to pneumococcal infection. TTP includes the triad of HUS in addition to fever and central nervous system (CNS) changes and is more common in older adolescents and adults.
  - b. DIC (see [Box 14-5](#))
5. **Other causes of thrombocytopenia:** Infection causing marrow suppression, malignancy, HIV, drug-induced thrombocytopenia, marrow

infiltration, cavernous hemangiomas (Kasabach-Merritt syndrome), thrombocytopenia with absent radii syndrome (TAR), thrombosis, hypersplenism, and other rare inherited disorders (e.g., Wiskott-Aldrich, Paris-Trousseau, Noonan, and DiGeorge syndromes; myosin 9– associated megaplatelet disorders; chromosomal abnormalities).

## V. COAGULATION (FIG. 14-2)

### A. Tests of Coagulation

An incorrect anticoagulant-to-blood ratio will give inaccurate results. Table 14-7 lists normal hematologic values for coagulation testing.

1. **Activated partial thromboplastin time (aPTT):** Measures intrinsic system; requires factors V, VIII, IX, X, XI, XII, fibrinogen, and prothrombin. May be prolonged in heparin administration, hemophilia, von Willebrand disease (v WD), DIC, and in the presence of circulating inhibitors (e.g., lupus anticoagulants).
2. **Prothrombin time (PT):** Measures extrinsic pathway; requires factors V, VII, X, fibrinogen, and prothrombin. May be prolonged in warfarin

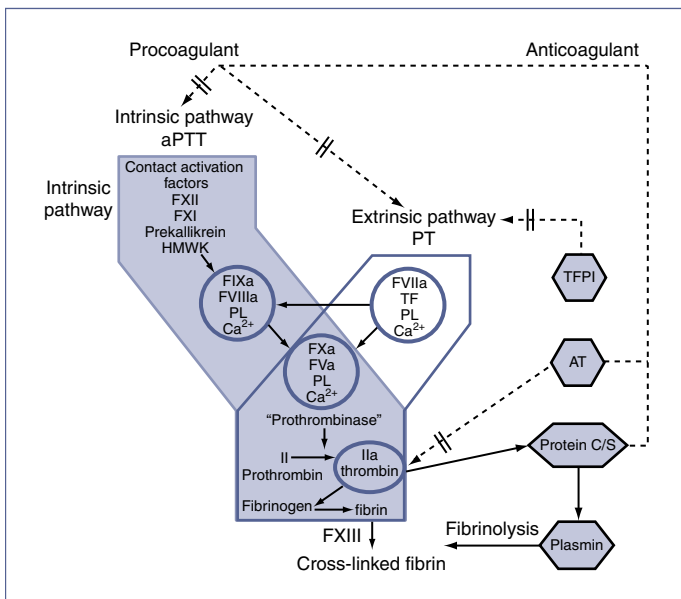


FIGURE 14-2

Coagulation cascade. AT, Antithrombin; F, factor; HMWK, high-molecular-weight kininogen; PL, phospholipid; TF, tissue factor; TFPI, tissue factor pathway inhibitor. (Adaptation courtesy James Casella and Clifford Takemoto.)

TABLE 14-7

## AGE-SPECIFIC COAGULATION VALUES

Coagulation Test	Preterm Infant (30–36 wk), Day of Life 1*	Term Infant, Day of Life 1	Day of Life 3	1 Month–1 yr	1–5 yr	6–10 yr	11–16 yr	Adult
PT (sec)	13.0 (10.6–16.2)	15.6 (14.4–16.4)	14.9 (13.5–16.4)	13.1 (11.5–15.3)	13.3 (12.1–14.5)	13.4 (11.7–15.1)	13.8 (12.7–16.1)	13.0 (11.5–14.5)
INR		1.26 (1.15–1.35)	1.20 (1.05–1.35)	1.00 (0.86–1.22)	1.03 (0.92–1.14)	1.04 (0.87–1.20)	1.08 (0.97–1.30)	1.00 (0.80–1.20)
aPTT (sec) <sup>†</sup>	53.6 (27.5–79.4)	38.7 (34.3–44.8)	36.3 (29.5–42.2)	39.3 (35.1–46.3)	37.7 (33.6–43.8)	37.3 (31.8–43.7)	39.5 (33.9–46.1)	33.2 (28.6–38.2)
Fibrinogen (g/L)	2.43 (1.50–3.73)	2.80 (1.92–3.74)	3.30 (2.83–4.01)	2.42 (0.82–3.83)	2.82 (1.62–4.01)	3.04 (1.99–4.09)	3.15 (2.12–4.33)	3.1 (1.9–4.3)
Bleeding time (min)*					6 (2.5–10)	7 (2.5–13)	5 (3–8)	4 (1–7)
Thrombin time (sec)	14 (11–17)	12 (10–16)*		17.1 (16.3–17.6)	17.5 (16.5–18.2)	17.1 (16.1–18.5)	16.9 (16.2–17.6)	16.6 (16.2–17.2)
Factor II (U/mL)	0.45 (0.20–0.77)	0.54 (0.41–0.69)	0.62 (0.50–0.73)	0.90 (0.62–1.03)	0.89 (0.70–1.09)	0.89 (0.67–1.10)	0.90 (0.61–1.07)	1.10 (0.78–1.38)
Factor V (U/mL)	0.88 (0.41–1.44)	0.81 (0.64–1.03)	1.22 (0.92–1.54)	1.13 (0.94–1.41)	0.97 (0.67–1.27)	0.99 (0.56–1.41)	0.89 (0.67–1.41)	1.18 (0.78–1.52)
Factor VII (U/mL)	0.67 (0.21–1.13)	0.70 (0.52–0.88)	0.86 (0.67–1.07)	1.28 (0.83–1.60)	1.11 (0.72–1.50)	1.13 (0.70–1.56)	1.18 (0.69–2.00)	1.29 (0.61–1.99)
Factor VIII (U/mL)	1.11 (0.50–2.13)	1.82 (1.05–3.29)	1.59 (0.83–2.74)	0.94 (0.54–1.45)	1.10 (0.36–1.85)	1.17 (0.52–1.82)	1.20 (0.59–2.00)	1.60 (0.52–2.90)
vWF (U/mL)*	1.36 (0.78–2.10)	1.53 (0.50–2.87)			0.82 (0.47–1.04)	0.95 (0.44–1.44)	1.00 (0.46–1.53)	0.92 (0.5–1.58)
Factor IX (U/mL)	0.35 (0.19–0.65)	0.48 (0.35–0.56)	0.72 (0.44–0.97)	0.71 (0.43–1.21)	0.85 (0.44–1.27)	0.96 (0.48–1.45)	1.11 (0.64–2.16)	1.30 (0.59–2.54)
Factor X (U/mL)	0.41 (0.11–0.71)	0.55 (0.46–0.67)	0.60 (0.46–0.75)	0.95 (0.77–1.22)	0.98 (0.72–1.25)	0.97 (0.68–1.25)	0.91 (0.53–1.22)	1.24 (0.96–1.71)
Factor XI (U/mL)	0.30 (0.08–0.52)	0.30 (0.07–0.41)	0.57 (0.24–0.79)	0.89 (0.62–1.25)	1.13 (0.65–1.62)	1.13 (0.65–1.62)	1.11 (0.65–1.39)	1.12 (0.67–1.96)
Factor XII (U/mL)	0.38 (0.10–0.66)	0.58 (0.43–0.80)	0.53 (0.14–0.80)	0.79 (0.20–1.35)	0.85 (0.36–1.35)	0.81 (0.26–1.37)	0.75 (0.14–1.17)	1.15 (0.35–2.07)
PK (U/mL)*	0.33 (0.09–0.57)	0.37 (0.18–0.69)			0.95 (0.65–1.30)	0.99 (0.66–1.31)	0.99 (0.53–1.45)	1.12 (0.62–1.62)
HMWK (U/mL)*	0.49 (0.09–0.89)	0.54 (0.06–1.02)			0.98 (0.64–1.32)	0.93 (0.60–1.30)	0.91 (0.63–1.19)	0.92 (0.50–1.36)
Factor XIIIa (U/mL)*	0.70 (0.32–1.08)	0.79 (0.27–1.31)			1.08 (0.72–1.43)	1.09 (0.65–1.51)	0.99 (0.57–1.40)	1.05 (0.55–1.55)
Factor XIIIs (U/mL)*	0.81 (0.35–1.27)	0.76 (0.30–1.22)			1.13 (0.69–1.56)	1.16 (0.77–1.54)	1.02 (0.60–1.43)	0.97 (0.57–1.37)
D-Dimer		1.47 (0.41–2.47)	1.34 (0.58–2.74)	0.22 (0.11–0.42)	0.25 (0.09–0.53)	0.26 (0.10–0.56)	0.27 (0.16–0.39)	0.18 (0.05–0.42)
FDPs*								Borderline titer = 1:25–1:50 Positive titer <1:50

TABLE 14-7

## AGE-SPECIFIC COAGULATION VALUES (Continued)

Coagulation Test	Preterm Infant (30–36 wk), Day of Life 1*	Term Infant, Day of Life 1	Day of Life 3	1 Month–1 yr	1–5 yr	6–10 yr	11–16 yr	Adult
<b>COAGULATION INHIBITORS</b>								
ATIII (U/mL)*	0.38 (0.14–0.62)	0.63 (0.39–0.97)			1.11 (0.82–1.39)	1.11 (0.90–1.31)	1.05 (0.77–1.32)	1.0 (0.74–1.26)
$\alpha_2$ -M (U/mL)*	1.10 (0.56–1.82)	1.39 (0.95–1.83)			1.69 (1.14–2.23)	1.69 (1.28–2.09)	1.56 (0.98–2.12)	0.86 (0.52–1.20)
C1-Inh (U/mL)*	0.65 (0.31–0.99)	0.72 (0.36–1.08)			1.35 (0.85–1.83)	1.14 (0.88–1.54)	1.03 (0.68–1.50)	1.0 (0.71–1.31)
$\alpha_2$ -AT (U/mL)*	0.90 (0.36–1.44)	0.93 (0.49–1.37)			0.93 (0.39–1.47)	1.00 (0.69–1.30)	1.01 (0.65–1.37)	0.93 (0.55–1.30)
Protein C (U/mL)	0.28 (0.12–0.44)	0.32 (0.24–0.40)	0.33 (0.24–0.51)	0.77 (0.28–1.24)	0.94 (0.50–1.34)	0.94 (0.64–1.25)	0.88 (0.59–1.12)	1.03 (0.54–1.66)
Protein S (U/mL)	0.26 (0.14–0.38)	0.36 (0.28–0.47)	0.49 (0.33–0.67)	1.02 (0.29–1.62)	1.01 (0.67–1.36)	1.09 (0.64–1.54)	1.03 (0.65–1.40)	0.75 (0.54–1.03)
<b>FIBRINOLYTIC SYSTEM*</b>								
Plasminogen (U/mL)	1.70 (1.12–2.48)	1.95 (1.60–2.30)			0.98 (0.78–1.18)	0.92 (0.75–1.08)	0.86 (0.68–1.03)	0.99 (0.7–1.22)
TPA (ng/mL)					2.15 (1.0–4.5)	2.42 (1.0–5.0)	2.16 (1.0–4.0)	4.90 (1.40–8.40)
$\alpha_2$ -AP (U/mL)	0.78 (0.4–1.16)	0.85 (0.70–1.0)			1.05 (0.93–1.17)	0.99 (0.89–1.10)	0.98 (0.78–1.18)	1.02 (0.68–1.36)
PAI (U/mL)					5.42 (1.0–10.0)	6.79 (2.0–12.0)	6.07 (2.0–10.0)	3.60 (0–11.0)

\*Data from Andrew M, Paes B, Milner R, et al. Development of the human anticoagulant system in the healthy premature infant. *Blood*. 1987;70:165–172; Andrew M, Paes B, Milner R, et al. Development of the human anticoagulant system in the healthy premature infant. *Blood*. 1988;72:1651–1657; and Andrew M, Vegh P, Johnston M, et al. Maturation of the hemostatic system during childhood. *Blood*. 1992;8:1998–2005.

†aPTT values may vary depending on reagent.

$\alpha_2$ -AP,  $\alpha_2$ -Antiplasmin;  $\alpha_2$ -AT,  $\alpha_2$ -antitrypsin;  $\alpha_2$ -M,  $\alpha_2$ -macroglobulin; aPTT, activated partial thromboplastin time; ATIII, antithrombin III; FDPs, fibrin degradation products; HMWK, high-molecular-weight kininogen; INR, international normalized ratio; PAI, plasminogen activator inhibitor; PK, prekallikrein; PT, prothrombin time; TPA, tissue plasminogen activator; VIII, factor VIII procoagulant; vWF, von Willebrand factor.

Adapted from Monagle P, Barnes C, Ignjatovic, V, et al. Developmental haemostasis. Impact for clinical haemostasis laboratories. *Thromb Haemost*. 2006;95:362–372.

administration, deficiencies of vitamin K–associated factors, malabsorption, liver disease, DIC, and the presence of circulating inhibitors.

3. **Platelet function testing:** Platelet aggregation and the Platelet Function Analyzer-100 (PFA-100) system are in vitro methods for measuring platelet function. Bleeding time (BT) evaluates clot formation, including platelet number and function and von Willebrand factor (vWF). Always assess the platelet number and history of ingestion of platelet inhibitors (e.g., nonsteroidal antiinflammatory drugs [NSAIDs]) before any platelet function testing.

## B. Hypercoagulable States

Present clinically as venous or arterial thrombosis (Box 14-2)

1. **Laboratory evaluation**<sup>4,5</sup>:
  - a. Initial laboratory screening includes PT and high-sensitivity aPTT; if PT or aPTT are prolonged, a mixing study to look for circulating anticoagulants.
  - b. Extended workup for hypercoagulable states (Box 14-3): A hematologist should be consulted.

### BOX 14-2

#### HYPERCOAGULABLE CONDITIONS

##### CONGENITAL

**Protein C and S deficiency:** Hereditary autosomal dominant disorder.

Heterozygotes have three- to sixfold increased risk for venous thrombosis.

**Antithrombin III deficiency:** Hereditary autosomal dominant disorder.

Homozygotes die in infancy.

**Factor V Leiden (activated protein C resistance):** 2%–5% of European whites are heterozygotes with two- to four-fold increased risk for venous thrombosis; 1 in 1000 are homozygotes, with 80- to 100-fold increased risk for venous thrombosis.

**Homocystinemia:** Increased levels of homocysteine associated with arterial and venous thromboses, often due to MTHFR abnormalities

**Others:** Prothrombin mutation (G20210A), plasminogen abnormalities, fibrinogen abnormalities

##### ACQUIRED

**Endothelial damage:** Causes include vascular catheters, smoking, diabetes, hypertension, surgery, hyperlipidemia.

**Hyperviscosity:** Macroglobulinemia, polycythemia, sickle cell disease

**Antiphospholipid antibodies:** Seen in patients with systemic lupus erythematosus or other autoimmune diseases; can occur with infections or idiopathically. Associated with venous and arterial thromboses and spontaneous abortions.

**Platelet activation:** Caused by essential thrombocytosis, oral contraceptives, heparin-induced thrombocytopenia

**Others:** Drugs, malignancy, liver disease, inflammatory disease such as inflammatory bowel disease, paroxysmal nocturnal hemoglobinuria, lipoprotein A



- c. Identification of one risk factor (e.g., indwelling vascular catheter) does not preclude the search for others, especially when accompanied by a family or personal history of thrombosis.
2. **Treatment of thromboses:**
- a. Unfractionated heparin (UFH): Used for treatment or prevention of deep venous thrombosis (DVT) or pulmonary embolism (PE), atrial fibrillation, mechanical heart valve, arterial thrombosis, cerebral sinovenous thrombosis, cardioembolic arterial ischemic stroke, homozygous purpura fulminans, and for bridge to warfarin therapy
- (1) See [Tables 14-8 to 14-11](#) for UFH bolus and drip adjustment guidelines for goal heparin anti-Xa level range of 0.3–0.7 U/mL or aPTT range 50–80 seconds.
  - (2) UFH may be reversed with protamine.
  - (3) UFH or low-molecular-weight-heparin (LMWH) therapy should continue for at least 5–7 days while initiating warfarin for treatment of venous thrombosis.
- Contraindications: Patients with known hypersensitivity to heparin, major active bleeding, known or suspected heparin-induced thrombocytopenia (HIT), or concurrent epidural therapy
- Precautions: Patients at high risk for bleeding (general bleeding precaution protocols must be implemented) or with platelet count

**BOX 14-3****EXTENDED WORKUP FOR HYPERCOAGULABLE STATES\*****Suggested tiered testing approach:****First Tier:**

Antithrombin III activity (antithrombin III deficiency and dysfunction)  
 Activated protein C resistance assay (screening test for factor V Leiden)  
 Factor V Leiden (DNA-based assay for factor V Leiden)  
 Factor II 20210A (prothrombin mutation)  
 Homocysteine  
 Methyltetrahydrofolate reductase (MTHFR) genetic testing if homocysteine elevated  
 Dilute Russell viper venom test (antiphospholipid antibody syndrome)  
 Anticardiolipin screening enzyme-linked immunosorbent assay (ELISA; anticardiolipin antibodies)  
 Protein C activity (protein C deficiency and dysfunction)  
 Protein S activity (protein S deficiency and dysfunction)  
 Factor VIII, IX, XI

**Second Tier (less common conditions):**

Platelet neutralization procedure (lupus anticoagulant)  
 Plasminogen activity  
 Tissue plasminogen activator (TPA) antigen  
 Plasminogen activator inhibitor activity (PAI-1; measures activity of this TPA inhibitor)  
 $\alpha_2$ -Antiplasmin activity (measures activity of this plasmin inhibitor)  
 Lipoprotein (a) (Lp[a]) promotes decreased fibrinolysis

\*Where necessary, abnormality tested for is listed in parentheses.

TABLE 14-8

**UNFRACTIONATED HEPARIN DOSE INITIATION GUIDELINES FOR GOAL aPTT RANGE OF 50–80 SECONDS\***

Age	Loading Dose ( <i>No Loading Dose for Stroke Patients</i> )	Initial Infusion Rate	Monitoring Parameters
Neonates and infants <1 yr	75 units/kg intravenously (IV)	28 units/kg/hr	Obtain aPTT 4 hr after loading dose.
Children ≥1 yr–16 yr	75 units/kg IV (max dose = 7700 units)	20 units/kg/hr (initial max rate = 1650 units/hr)	Obtain aPTT 4 hr after loading dose.
Patients >16 yr	70 units/kg (max dose = 7700 units)	15 units/kg/hr (initial max rate = 1650 units/hr)	Obtain aPTT 4 hr after loading dose.

\*Reflects antifactor Xa level of 0.3–0.7 IU/mL with current activated partial thromboplastin time (aPTT) reagents at Johns Hopkins Hospital 2/3/11. Therapeutic aPTT range may vary with different aPTT reagents.

TABLE 14-9

**UNFRACTIONATED HEPARIN DOSE ADJUSTMENT ALGORITHM FOR GOAL aPTT RANGE OF 50–80 SECONDS\***

aPTT (seconds)	Bolus (units/kg)	Hold (minutes)	Rate Change	Repeat aPTT (hours)
≤39	50	0	Increase 20%	4 hr
40–49	0	0	Increase 10%	4 hr
50–80	0	0	0	4 hr, then next day once two consecutive values are in range
81–100	0	0	Decrease 10%	6 hr
101–125	0	30–60 min	Decrease 20%	6 hr
≥125†	0	60–120 min until aPTT <115 sec	Decrease 30%; restart when aPTT <115 sec	6 hr after infusion is restarted

\*Reflects antifactor Xa level of 0.3–0.7 IU/mL with current activated partial thromboplastin (aPTT) reagents at Johns Hopkins Hospital 2/3/11. Therapeutic aPTT range may vary with different aPTT reagents.

†Confirm that specimen was not drawn from heparinized line or same extremity as site of heparin infusion.

TABLE 14-10

**UNFRACTIONATED HEPARIN DOSE INITIATION GUIDELINES FOR GOAL ANTI-Xa ACTIVITY OF 0.3-0.7 UNITS/ML**

Age	Loading Dose ( <i>No Bolus for Stroke Patients</i> )	Initial Infusion Rate	Monitoring Parameters
Neonates and infants <1 year	75 units/kg IV	28 units/kg/hr	Obtain anti-Xa 4 hours after loading dose
Children ≥1 year–16 years	75 units/kg IV (max dose = 7700 units)	20 units/kg/hr (max rate = 1650 units/hour)	Obtain anti-Xa 4 hours after loading dose
Patients > 16 years	70 units/kg (max dose = 7700 units)	15 units/kg/hr (max rate = 1650 units/hr)	Obtain anti-Xa 4 hours after loading dose

TABLE 14-11

**UNFRACTIONATED HEPARIN DOSE ADJUSTMENT ALGORITHM FOR GOAL ANTI-Xa ACTIVITY OF 0.3–0.7 UNITS/ML**

Anti-Xa level	Bolus (units/kg)	Hold (minutes)	Rate Change	Repeat anti-Xa (hours)
≤0.1	50	0	Increase 20%	4 hr
0.2	0	0	Increase 10%	4 hr
0.3–0.7	0	0	0	4 hr, then next day once two consecutive values are in range
0.8–0.9	0	0	Decrease 10%	6 hr
1.0–1.1	0	30–60	Decrease 20%	6 hr
>1.2*	0	60–120 until anti-Xa <1.0	Decrease 30%; restart when anti-Xa activity <1.0	6 hr after infusion is restarted

\*Confirm that specimen was not drawn from heparinized line or same extremity as site of heparin infusion.

<50,000/mm<sup>3</sup>. Avoid intramuscular injections and avoid other drugs that affect platelet function (e.g., NSAIDs, aspirin, clopidogrel). Baseline labs prior to institution of UFH therapy (to assess baseline coagulation state): aPTT, PT, BMP, Heme-8.

- b. LMWH<sup>4,5</sup>: Administered subcutaneously, has a longer half-life, more predictable pharmacokinetics, and requires less monitoring. Also associated with lower risk for HIT.
  - (1) Dose depends on preparation. See Formulary for enoxaparin dosage information.
  - (2) Monitor LMWH therapy by following anti-Xa activity. Therapeutic range is 0.5–1.0 U/mL for thrombosis treatment and 0.1–0.3 U/mL for prophylactic dosing. Blood for anti-Xa activity should be drawn 4 hours after dose.
  - (3) LMWH-induced bleeding can be partially reversed with protamine. Consult hematologist for protamine reversal protocol.
- c. Warfarin: Used for long-term anticoagulation. Patient should receive heparin (UFH or LMWH) while initiating warfarin therapy, owing to possibility of hypercoagulability from decreased protein C and S levels.
  - (1) Usually administered orally at an initiation dose for 1–2 days, followed by a daily dose sufficient to maintain the PT/INR in the desired range. Infants often require higher daily doses. Levels should be measured every 1–4 weeks. Table 14-12 lists dose adjustment guidelines, and Table 14-13 outlines management of excessive anticoagulation.
  - (2) Efficacy is greatly affected by dietary intake of vitamin K. Patients should receive appropriate dietary education.
  - (3) Box 14-4 lists medications that influence warfarin therapy.
- d. Anticoagulant therapy alters many coagulation tests:
  - (1) Heparin prolongs aPTT, thrombin time, dilute Russell Viper Venom test (dRVVT), and mixing studies.

TABLE 14-12

**ADJUSTMENT AND MONITORING OF WARFARIN TO MAINTAIN AN INTERNATIONAL NORMALIZED RATIO (INR) BETWEEN 2 AND 3<sup>\*,11</sup>****I. DAY 1 INITIAL DOSING**

1. Newborn: for age <3 mo, there are limited data for safety and efficacy of warfarin. Higher dose may be needed in neonates and infants.
2. Infants and children:
  - If baseline INR is 1–1.3, dose = 0.2 mg/kg/dose orally Q24 hr (max 7.5 mg/dose)<sup>‡</sup>
  - If baseline INR >1.3, liver dysfunction, postoperative cardiac Fontan procedure patients, NPO/poor nutrition, receiving broad-spectrum antibiotics, receiving medications causing significant drug/drug interactions, receiving medications with CYP2C9 enzyme inhibition (e.g., amiodarone, metronidazole, fluconazole, Bactrim), or slow metabolizer of warfarin, dose = 0.1 mg/kg/dose Q24 hr (max 5 mg/dose)

**II. DAYS 2–4****Dose Adjustment for Goal INR of 2–3**

Day 2		Day 3 and 4	
INR Level	Action	INR Level	Action
1.1–1.3	Repeat initial dose	1.1–1.3	Repeat initial dose <sup>*</sup>
1.4–1.9	50% of initial dose	1.4–1.9	50% of initial dose <sup>*</sup>
≥2	Hold dose for 24 hr, then restart at 50% of initial dose	2–3	50% of initial dose <sup>†</sup>
		3.1–3.5	25% of initial dose <sup>†</sup>
		>3.5	Hold dose until INR <3.5, then restart at 50% of previous dose <sup>†</sup>

**III. DAY 5 AND MAINTENANCE****Maintenance Dosing**

≥5 Days	
INR Level	Action
1.1–1.4	Increase weekly dose by 20%
1.5–1.9	Increase weekly dose by 10%
2–3	Continue current dose
3.1–3.5	Decrease weekly dose by 10%
>3.5	Hold dose, recheck INR daily until INR <3.5, then restart at 20% less than previous dose

<sup>\*</sup>If INR is not >1.5 on day 4, patient should be reassessed, and dose/kg should be adjusted on an individual basis.

<sup>†</sup>Consult pediatric hematology for patient-specific recommendations on reduced dosing.

<sup>‡</sup>Reported average daily dose to maintain INR of 2–3 for infants is 0.33 mg/kg; for adolescents, 0.09 mg/kg; and for adults, from 0.04–0.08 mg/kg.

Adapted from The Johns Hopkins Hospital Children's Center pediatric policies, procedures, and protocols general care (Policy Number GEN069), Baltimore, 2010.

TABLE 14-13

## MANAGEMENT OF EXCESSIVE WARFARIN ANTICOAGULATION

INR <5 without serious bleeding	Hold warfarin. Recheck INR daily. When INR approaches therapeutic range, resume warfarin at lower dose and follow INR daily.*
INR ≥5 but <8 without serious bleeding	Hold warfarin. Recheck INR every 12–24 hr. If high risk for bleeding, consider low dose of vitamin K oral or IV (30 mcg/kg for patients <40 kg in weight; 1–2.5 mg for patients >40 kg). When INR approaches therapeutic range, resume warfarin at a lower dose.*
INR ≥8 without serious bleeding	Hold warfarin. Recheck INR every 6–12 hr. Give vitamin K orally (PO) or IV (30 mcg/kg for patients <40 kg in weight; 1–2.5 mg for patients >40 kg). INR reduction expected to occur within 12–24 hours with IV or 24–48 hours with PO vitamin K. Repeat vitamin K as necessary. When INR approaches therapeutic range, resume warfarin at a lower dose.*
Serious bleeding at any INR elevation	Hold warfarin. Monitor INR every 6 hr. Give vitamin K IV (2.5–5 mg). Vitamin K may be repeated as needed. Consider use of FFP (10–15 mL/kg IV), recombinant factor VIIa (16 mcg/kg IV), prothrombinase complex concentrate, or rhFVIIa (Novoseven) IV. Restart warfarin when INR approaches therapeutic range and when clinically appropriate at a lower dose.*
Life-threatening bleeding at any INR	Hold warfarin. Monitor INR every 2–4 hr. Administer vitamin K IV at 5–10 mg. Repeat vitamin K as needed. Transfuse FFP (10–15 mL/kg IV), consider rhFVIIa (Novoseven) or prothrombinase complex concentrate. Restart warfarin when INR approaches therapeutic range and when clinically appropriate at a lower dose.*

\*Refer to Table 14-12.

**NOTE:** Always evaluate for bleeding risks and potential drug interactions.

FFP, Fresh frozen plasma; INR, international normalized ratio; IV, intravenous; rhVIIa, activated recombinant human factor VII.

Adapted from The Johns Hopkins Hospital Children's Center pediatric policies, procedures, and protocols general care (Policy Number GEN069), Baltimore, 2010.

(2) Warfarin prolongs PT, aPTT, and dRVVT. Warfarin reduces the activity of vitamin K–dependent factors (II, VII, IX, X, protein C and S).

e. Thrombolytic therapy should be considered for life- or limb-threatening thrombosis. Consult a hematologist.

**NOTE:** Children receiving anticoagulation therapy should be protected from trauma. Subcutaneous injections should be used when possible, and caution should be used with intramuscular injections. The use of antiplatelet agents and arterial punctures should be avoided.

## BOX 14-4

## MEDICATIONS THAT INFLUENCE WARFARIN THERAPY\*

SIGNIFICANT INCREASE IN INR	SIGNIFICANT DECREASE IN INR
Amiodarone	Amobarbital
Anabolic steroids	Aprepitant
Bactrim (TMP/SMZ)	Butabarbital
Chloramphenicol	Carbamazepine
Disulfiram	Dicloxacillin
Fluconazole	Griseofulvin
Isoniazid	Methimazole
Metronidazole	Phenobarbital
Miconazole	Phenytoin
Phenylbutazone	Primidone
Quinidine	Propylthiouracil
Sulfinpyrazone	Rifabutin
Sulfisoxazole	Rifampin
Tamoxifen	Secobarbital
MODERATE INCREASE IN INR	MODERATE DECREASE IN INR
Cimetidine	Atazanavir
Ciprofloxacin	Efavirenz
Clarithromycin	Nafcillin
Delavirdine	Ritonavir
Efavirenz	
Itraconazole	
Lovastatin	
Omeprazole	
Propafenone	
Ritonavir	

INR, International normalized ratio; TMP/SMZ, trimethoprim/sulfamethoxazole.

\*Numerous medications not listed in this table can affect warfarin administration.

### C. Bleeding Disorders (Fig. 14-3 and Box 14-5)

1. **Differential diagnosis of bleeding disorders** (Table 14-14 and Box 14-5)
2. **Desired factor replacement goals in hemophilia** (Table 14-15)

## VI. BLOOD COMPONENT REPLACEMENT

### A. Blood Volume

Requirements are age specific (Table 14-16).

### B. Blood Product Components

1. **RBCs:** Decision to transfuse RBCs should be made with consideration of clinical symptoms and signs, degree of cardiorespiratory or CNS disease, cause and course of anemia, and options for alternative therapy, noting risks for transfusion-associated infections and reactions.

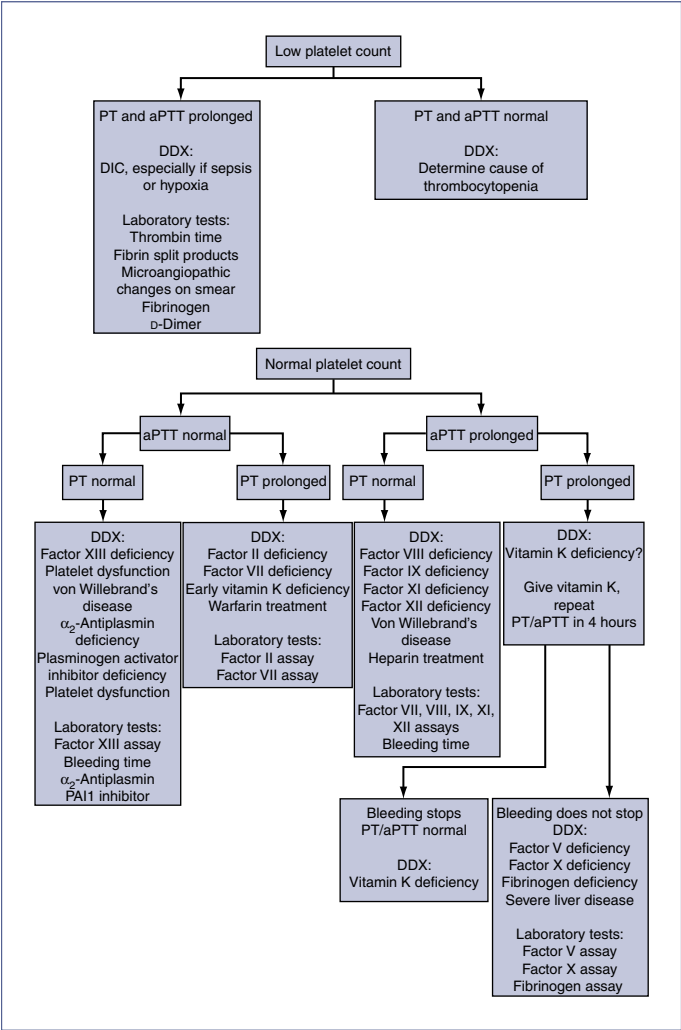


FIGURE 14-3

Differential diagnosis (DDX) of bleeding disorders. aPTT, Activated partial thromboplastin time; DIC, disseminated intravascular coagulation; PT, prothrombin time.

**ACQUIRED COAGULOPATHIES**

**Disseminated intravascular coagulation:** Characterized by prolonged PT and aPTT, decreased fibrinogen and platelets, increased fibrin degradation products, and elevated D-dimer. Treatment includes identifying and treating underlying disorder. Replacement of depleted coagulation factors with FFP may be necessary in severe cases, especially when bleeding is present; 10–15 mL/kg will raise clotting factors 20%. Fibrinogen, if depleted, can be given as cryoprecipitate. Platelet transfusions may also be necessary.

**Liver disease:** Liver is the major site of synthesis of factors V, VII, IX, X, XI, XII, XIII, prothrombin, plasminogen, fibrinogen, protein C and S, and ATIII. Treatment with FFP and platelets may be needed, but this will increase hepatic protein load. Vitamin K should be given to patients with liver disease and clotting abnormalities.

**Vitamin K deficiency:** Factors II, VII, IX, X, protein C, and protein S are vitamin K dependent. Early vitamin K deficiency may present with isolated prolonged PT because factor VII has the shortest half-life. Fibrinogen should be normal.

aPTT, Activated partial thromboplastin time; CNS, central nervous system; DIC, disseminated intravascular coagulation; FFP, fresh frozen plasma; PT, prothrombin time.

**TABLE 14-14****COMMON COAGULATION DISORDERS****Factor VIII deficiency (hemophilia A)\***

Characteristics: X-linked recessive, prolonged aPTT, reduced factor VIII activity, normal PT and BT

Treatment:

- Treat with factor VIII concentrate, preferably recombinant factor VIII to reduce risk of infection.
- Factor level recovers by 2% per 1 unit of factor VIII per kg of body weight (refer to [Table 14-15](#)).
- First dose has shorter half-life, so if redosing needed, second dose should be given after 4–8 hr. Subsequent doses can be given every 12 hr.
- Continuous infusion often desirable—example, surgical patients or those requiring prolonged therapy usually need 50 U/kg loading dose, followed by 3–5 U/kg/hr.
- For suspected intracranial bleeding, replace to 100% **before** diagnostic procedure (e.g., computed tomography [CT] scan).
- Dose calculation: units of factor VIII needed = weight (kg) × desired % replacement × 0.5.

**Factor IX deficiency (hemophilia B or Christmas disease)\***

Characteristics: X-linked recessive, prolonged aPTT, reduced factor IX activity

Treatment:

- Treat with factor IX concentrate, preferably recombinant to reduce risk of infection.
- Factor level usually recovers by 1% for each unit of factor IX concentrate per kg of body weight.
- Half-life of factor IX 18–24 hr. Similar to factor VIII, if second dose needed, it should be given at a shorter interval.
- Recombinant factor IX has a shorter half-life; consider evaluation of in vivo factor survival in patient.
- Replace to 100% **before** diagnostic procedure if intracranial bleeding is suspected.
- Dose calculation: units of factor IX needed = weight (kg) × desired % replacement (may be advisable to multiply by 1.2 for recombinant factor IX).



TABLE 14-14

## COMMON COAGULATION DISORDERS (Continued)

**von Willebrand disease**

Characteristics: vWF binds platelets to subendothelial surfaces and carries and stabilizes factor VIII.

Type 1: Decreased activity of vWF and proportionally decreased quantity of vWF. Mild to moderate bleeding. Prolonged BT, normal platelet count, platelet dysfunction on platelet function testing, aPTT normal in most cases but may be mildly prolonged.

Type 2: Characterized by four subtypes, all with various functional abnormalities of vWF. Mild to moderate bleeding but in some cases can be severe.

Type 3: Absence or near absence of vWF, with reduction of factor VIII and severe bleeding.

Treatment:

- Majority of patients with type 1 vWD respond to DDAVP (desmopressin acetate) with increases in vWF activity from two- to threefold over baseline (DDAVP responsiveness should be established by prior testing). IV or intranasal DDAVP may be used for minor bleeding or surgical procedures.
- DDAVP may be contraindicated in the rare vWD type 2B, because it may exacerbate thrombocytopenia.
- For more severe disease or patients who do not respond to DDAVP, treatments of choice are purified plasma-derived products containing both vWF and factor VIII (HUMATE P, Alphanate, or Wilate). These concentrates are preferred because they are virally inactivated.
- Aminocaproic acid 100 mg/kg IV or PO every 4–6 hr (up to 30 g/day) may be useful for treatment of mucosal bleeding and as prophylaxis for dental extraction.

\*All patients with hemophilia should be vaccinated with hepatitis A and B vaccines.

aPTT, Activated partial thromboplastin time; BT, bleeding time; IV, intravenous; PO, per os; PT, prothrombin time; vWF, von Willebrand factor.

TABLE 14-15

## DESIRED FACTOR REPLACEMENT IN HEMOPHILIA

Bleeding Site	Desired Level (%)
Minor soft tissue bleeding	20–30
Joint	40–70
Simple dental extraction	50
Major soft tissue bleeding	80–100
Serious oral bleeding	80–100
Head injury	100+
Major surgery (dental, orthopedic, other)	100+

**NOTE:** A hematologist should be consulted for all major bleeding and before surgery.

Round to the nearest vial; do not exceed 200%.

- a. Packed RBC (PRBC) transfusion: Concentrated RBCs with HCT of 55%–70%. A typed and cross-matched blood product is preferred when possible; O-negative (or O-positive) blood may be used if transfusion cannot be delayed. O-negative is preferred for females of childbearing age to reduce risk for Rh sensitization.

- (1) Unless rapid replacement is required for acute blood loss or shock, infuse no faster than 2–3 mL/kg/hr (generally 10–15 mL/kg aliquots over 4 hr) to avoid congestive heart failure.
- (2) Rule of thumb in severe compensated anemia: Give an  $X$  mL/kg aliquot, where  $X$  = patient Hb (g/dL); for example, if Hb = 5 g/dL, transfuse 5 mL/kg over 4 hours.
- (3) To calculate the volume of PRBC to achieve a desired HCT, use the following equation:

$$\text{Volume of PRBCs (mL)} = \frac{\text{EBV (mL)} \times (\text{desired HCT} - \text{actual HCT})}{\text{HCT of PRBCs}}$$

where EBV is the estimated blood volume (see Table 14-16 for age-specific EBV) and HCT of PRBCs is usually 55%–70%

- (4) A unit of blood is 500 mL, but approximately 300 mL after processing without significant loss of red cells. This may vary with type of diluents used and time of storage, owing to red cell compaction.

- b. Leukocyte-poor PRBCs:

- (1) Filtered RBCs: 99.9% of WBCs removed from product; used for cytomegalovirus (CMV)-negative patients to reduce risk for CMV transmission. Also reduces likelihood of a nonhemolytic febrile transfusion reaction.
- (2) Washed RBCs: 92%–95% of WBCs removed from product. Similar advantages to leukocyte-poor filtered RBCs. Although filtered leukocyte-poor blood is now more commonly used, washing may be helpful if a patient has preexisting antibodies to blood products (e.g., patients who have complete IgA deficiency or history of urticarial transfusion reactions).

TABLE 14-16

## ESTIMATED BLOOD VOLUME (EBV)

Age	Total Blood Volume (mL/kg)
Preterm infants	90–105
Term newborns	78–86
1–12 mo	73–78
1–3 yr	74–82
4–6 yr	80–86
7–18 yr	83–90
Adults	68–88

Data from Nathan D, Oski FA. *Hematology of Infancy and Childhood*. Philadelphia: WB Saunders, 1998.

- c. Irradiated blood products:
- (1) Many blood products (PRBCs, platelet preparations, leukocytes, FFP, and others) contain viable lymphocytes capable of proliferation and engraftment in the recipient, causing graft-versus-host disease (GVHD). Irradiation with 1500 cGy before transfusion may prevent GVHD but does not prevent antibody formation against donor white cells. Engraftment most likely in young infants, immunocompromised patients, and patients receiving blood from first-degree relatives.
  - (2) Indications: Intensive chemotherapy, leukemia, lymphoma, bone marrow transplantation, solid organ transplantation, known or suspected immune deficiencies, intrauterine transfusions, and transfusions in neonates.
- d. CMV-negative blood: Obtained from donors who test negative for CMV. May be given to neonates or other immunocompromised patients, including those awaiting organ or marrow transplant who are CMV negative.
2. **Platelets:** Indicated to treat severe or symptomatic thrombocytopenia. Should not be refrigerated because this promotes premature platelet activation and clumping. Bacteremia secondary to contamination more common than with refrigerated blood products.
- a. Single-donor product: Preferred over pooled concentrate for patients with antiplatelet antibodies.
  - b. Leukocyte-poor: Use if there is a history of significant acute febrile platelet transfusion reactions.
  - c. Usually give 4 U/m<sup>2</sup>, or approximately 10 mL/kg of normally concentrated platelet product. Platelet count is raised by 10,000 to 15,000/μL by giving 1 U/m<sup>2</sup>. For infants and children, 10 mL/kg will increase platelet count by about 50,000/μL.
  - d. Hemorrhagic complications are rare with platelet counts >20,000/μL. A transfusion *trigger* of 10,000/μL is recommended by many in the absence of serious bleeding complications. Platelet count >50,000/μL is advisable for minor procedures; >100,000/μL is advisable for major surgery or intracranial operation.
  - e. Usually unit = 50 mL after processing,  $\geq 5.5 \times 10^{11}$  plt/unit.
3. **FFP:** Contains all clotting factors except platelets. Used in severe clotting factor deficiencies with active bleeding or in combination with vitamin K to achieve rapid reversal of effects of warfarin. Also replaces anticoagulant factors (antithrombin III, protein C, protein S). Used in treatment of DIC, vitamin K deficiency with active bleeding, or TTP. One milliliter of FFP expected to provide 1 unit of activity of all factors except labile factor V and VIII, but individual units may vary. Usual amount is 10–15 mL/kg; repeat doses as needed. In acquired TTP, plasma exchange is the treatment of choice. Usually unit = 250–300 mL after processing.

4. **Cryoprecipitate:** Enriched for factor VIII (5–10 U/mL), vWF, and fibrinogen. Historically useful for children with factor VIII or vWF deficiency in the context of active bleeding, but concentrates or recombinant products now preferred because of lower risk for viral transmission. Useful for raising fibrinogen when small volumes are required. Usually unit = 10–15 mL after processing (80 units factor VIII and 250 mg fibrinogen).
5. **Monoclonal factor VIII:** Highly purified factor derived from pooled human blood using monoclonal antibodies.
6. **Recombinant factor VIII or IX:** Highly purified with less (theoretical) infectious risk than pooled human products. There is risk for inhibitor formation, as with other products.

### C. PRBC Exchange Transfusion

1. **Partial PRBC exchange transfusion may be indicated** for sickle cell patients with acute chest syndrome, stroke, intractable pain crisis, or refractory priapism. Replace with Sickledex-negative cells. Follow HCT carefully during transfusion to avoid hyperviscosity, maintaining HCT <35%.
2. **Indications for double packed volume PRBC exchange transfusion** include severe acute chest and CVA. This is based on twice the patient's calculated packed cell volume. Goal is to reduce percentage of HbS to <30%. Expected reduction in percentage of circulating sickle cells is 60%–80%.
3. **To calculate the volume of PRBC needed for a double packed volume PRBC exchange, use the following equation:**

$$\text{Desired volume of exchange} = \text{EBV (mL)} \times \frac{\text{Patient HCT} \times 2}{(\text{HCT of PRBC})}$$

where EBV is the age-dependent estimated blood volume (see [Table 14-16](#)), and HCT of PRBC is 55%–70%.

### D. Complications of Transfusions

1. **Acute transfusion reactions:**
  - a. Acute hemolytic reaction: most often the result of blood group incompatibility. Signs and symptoms include fever, chills, tachycardia, hypotension, and shock. Treatment includes immediate cessation of blood transfusion and institution of supportive measures. Laboratory findings include DIC, hemoglobinuria, and positive Coombs test.
  - b. Febrile nonhemolytic reaction: Usually the result of inflammatory cytokines; common in previously transfused patients. Symptoms include fever, chills, and diaphoresis. Stop transfusion and evaluate. Prevention includes premedication with antipyretics, antihistamines, corticosteroids, and if necessary, use of leukocyte-poor PRBCs.
  - c. Urticarial reaction: Reaction to donor plasma proteins. Stop transfusion immediately; treat with antihistamines, and epinephrine and steroids

if there is respiratory compromise (see also treatment of anaphylaxis, Chapter 1). Use washed or filtered RBCs with the next transfusion.

- d. Evaluation of acute transfusion reaction:
  - (1) Patient's urine: Test for hemoglobin.
  - (2) Patient's blood: Confirm blood type, screen for antibodies, and repeat direct Coombs test (DCT) on pretransfusion and posttransfusion sera.
  - (3) Donor blood: Culture for bacteria.
2. **Delayed transfusion reaction:** Usually due to minor blood group antigen incompatibility, with low or absent titer of antibodies at time of transfusion. Occurs 3–10 days after transfusion. Symptoms include fatigue, jaundice, and dark urine. Laboratory findings include anemia, positive Coombs test, new RBC antibodies, and hemoglobinuria. The need for acute intervention is much less likely than with acute reactions.
3. **Transmission of infectious diseases**<sup>6,10</sup>: Blood supply is tested for HIV types 1 and 2, HTLV types I and II, hepatitis B, hepatitis C, syphilis, and West Nile virus. Data from *2009 Red Book* estimate the risk for transmitting infection (estimated per unit) as follows: HIV (1 in 2,000,000); HTLV (1 in 641,000); hepatitis B (1 in 63,000–500,000); hepatitis C (1 in 100,000); parvovirus (1 in 10,000). CMV, hepatitis A, parasitic, tickborne, and prion diseases may also be transmitted by blood products.
4. **Sepsis:** Occurs with products contaminated with bacteria, particularly platelets, because they are stored at room temperature. Risk for transmitting bacteria in PRBCs is 1 in 5 million units, and in platelets is 1 in 100,000.

#### **E. Reasons Not to Consider a Directed Donor**

1. **Donors less likely to be truthful about risk**
2. **Increase risk of transfusion-related GVHD if from a relative**
3. **Can alloimmunize if potential bone marrow donor**

#### **F. Reasons to Consider a Directed Donor**

1. **Chronic transfusion programs** (e.g., thalassemia or sickle cell disease), where donors provide antigen-matched red cells repetitively for the same patient
2. **NAIT**, where maternal platelets lack causative antigens and represent optimal therapy

## **VII. INTERPRETING BLOOD SMEARS**

See Figures 14-4 through 14-15 for examples of blood smears. Examine the blood smear in an area where the RBCs are nearly touching but do not overlap.

### **A. RBC**

Examine size, shape, and color.

## B. WBC

A rough estimate of the WBC count can be made by looking at the smear under high power ( $\times 100$  magnification). Each one cell per high-power field correlates with approximately 500 WBC/mm<sup>3</sup> ( $\times 20$  magnification).

## C. Platelets

A rough estimate of platelet count is one platelet per high-power field corresponds to 10,000–15,000/ $\mu$ L. Platelet clumps usually indicate  $>100,000$  platelets/ $\mu$ L.

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# Chapter 15

## Immunology and Allergy

*Emily Braun, MD*

### I. ALLERGIC RHINITIS<sup>1-4</sup>

#### A. Epidemiology

1. **Most common chronic condition:** Affects 10%–30% of children
2. **Significant impact on quality of life,** including school performance and sleep patterns, as demonstrated in multiple studies
3. **Increases risk for** recurrent otitis media, asthma, acute and chronic sinusitis
4. **Risk factors:** Atopic family history, serum immunoglobulin (Ig) E >100 IU/mL before age 6 years, higher socioeconomic status, maternal smoke exposure in first year of life

#### B. Diagnosis

##### 1. History:

- a. Allergen-driven mucosal inflammation leading to cyclical exacerbations or persistent symptoms
- b. Symptoms: Nasal (congestion, rhinorrhea, pruritus), ocular (pruritus, tearing), postnasal drip (sore throat, cough, pruritus)
- c. Patterns: Seasonal (depending on local allergens) vs. perennial (with seasonal peaks)
- d. Coexisting atopic diseases common (eczema, asthma, food allergy)

##### 2. Physical examination:

- a. Allergic facies with shinners, mouth breathing, transverse nasal crease (“allergic salute”), accentuated lines below lower eyelids (Dennie-Morgan lines)
- b. Nasal mucosa may be normal to pink to pale gray, ± swollen turbinates.
- c. Injected sclera with or without clear discharge, conjunctival cobblestoning

##### 3. Diagnostic studies:

- a. Diagnosis can be made on clinical grounds, but skin testing can be confirmatory.
- b. Skin testing: Gold standard, determination of specific IgE involved
- c. Total IgE: Nonspecific, limited value
- d. Peripheral blood eosinophil count: Not sensitive enough to be diagnostic
- e. Nasal smear for eosinophils: Quick, easy screen with good positive predictive value
- f. Measurement of specific IgE: Identifies presence of serum IgE to selected antigens
- g. Imaging studies: Not useful
- h. Consider sleep study to evaluate for obstructive sleep apnea and pulmonary function tests (PFT) to evaluate for asthma.

### C. Differential Diagnosis

1. **Vasomotor rhinitis:** Symptoms made worse by scents, alcohol, or changes in temperature or humidity
2. **Infectious rhinitis:** Viral vs. bacterial
3. **Episodic rhinitis:** Allergic nasal symptoms elicited by sporadic exposures to inhaled aeroallergens
4. **Adenoid hypertrophy**
5. **Rhinitis medicamentosa:** Rebound rhinitis from prolonged use of nasal vasoconstrictors
6. **Sinusitis:** Acute or chronic
7. **Nonallergic rhinitis with eosinophilia syndrome (NARES)**
8. **Nasal polyps**

### D. Treatment

1. **Allergen avoidance:**
  - a. Relies on identification of triggers, most common of which are pollens, fungi, dust mites, insects, animals
  - b. Difficult to avoid ubiquitous airborne allergens
  - c. HEPA filter use may be of use when animal allergens are a concern
  - d. Thorough housecleaning and allergy-proof bed coverings can be useful
2. **Oral antihistamines** (diphenhydramine, cetirizine):
  - a. First-line treatment
  - b. Second-generation preparations preferable (loratadine, desloratadine, fexofenadine, cetirizine, levocetirizine)
  - c. Adverse effects: Sedation and anticholinergic side effects more prominent with first-generation agents
3. **Intranasal corticosteroids** (fluticasone, mometasone, budesonide, flunisolide, ciclesonide, triamcinolone):
  - a. Second-line treatment
  - b. Most effective maintenance therapy for nasal congestion
  - c. Potential benefit for ocular symptoms
  - d. No proven adverse effect on long-term growth
  - e. Adverse effects: nasal irritation, sneezing, bleeding
  - f. Recognize potential risk of adrenal suppression at high doses of inhaled or intranasal steroids
4. **Leukotriene inhibitors** (montelukast): Alone or in combination with antihistamines
5. **Mast cell stabilizers** (intranasal cromolyn):
  - a. Inexpensive and easily available
  - b. Most effective as prophylaxis
  - c. Few adverse effects
6. **Intranasal antihistamines** (azelastine, olopatadine):
  - a. Effective for acute symptoms
  - b. Not studied in children younger than 5 years
  - c. Adverse effects: Bitter taste, systemic absorption with sedation



7. **Anticholinergics** (ipratropium):
  - a. Useful for rhinorrhea only
  - b. Adverse effects: Drying of nasal mucosa
8. **Immunotherapy:**
  - a. Success rate is high when patients are chosen carefully and when performed by an allergy specialist.
  - b. Consider when drug side effects are limiting or triggering allergens are difficult to avoid.
  - c. Not recommended for patients with poor adherence to therapy or those with poorly-controlled asthma
  - d. Not well studied in children younger than 5 years
  - e. May reduce risk for future development of asthma, and treatment of allergic rhinitis may improve asthma control.
9. **Nasal rinsing with hypertonic saline:** Tolerable and inexpensive
10. **Ophthalmic agents:** Can be used to treat allergic conjunctivitis ([Table 15-1](#)). Up to 60% of patients with allergic rhinitis have concomitant conjunctivitis.

TABLE 15-1

**EXAMPLES OF OPHTHALMIC AGENTS INDICATED FOR TREATMENT OF ALLERGIC CONJUNCTIVITIS**

Brand Name	Ingredient	Dose
Alocril ( $\geq 3$ yr) Sol: 5 mL	Nedocromil sodium 2% (mast cell stabilizer), benzalkonium chloride	1–2 drops several times a day; remove contact lenses during therapy
Patanol/Pataday ( $\geq 3$ yr) Sol: 5 mL	Olopatadine 0.1% ( $H_1$ -antagonist and mast cell stabilizer)	1 drop once daily–BID
Zaditor ( $\geq 3$ yr) Sol: 5 mL	Ketotifen fumarate 0.025% ( $H_1$ -antagonist and mast cell stabilizer)	1 drop Q8–12 hr

**II. FOOD ALLERGY <sup>1-3</sup>**
**A. Epidemiology**

1. **Prevalence is 6%–8% in pediatric population**
2. **Most common allergens in children:** Milk, eggs, peanuts, tree nuts (e.g., cashew, walnut), soy, wheat

**B. Manifestations of Food Allergy:**

1. **Often a combination of several syndromes;** symptoms can occur within minutes to hours of ingesting food.
2. **Diagnosis requires** both sensitization (demonstration of allergen-specific IgE) and clinical symptoms after exposure to allergen.
3. **Rarely presents with isolated respiratory symptoms.**
4. **Anaphylaxis:** see Chapter 1, Allergic Emergencies (Anaphylaxis)
5. **Skin syndromes:**
  - a. Urticaria/angioedema:
    - (1) Chronic urticaria is rarely related to food allergy.
    - (2) Acute urticaria due to food allergy predicts risk for future anaphylaxis.

- b. Atopic dermatitis/eczema:
  - (1) Food allergy is more common in patients with atopic dermatitis.
  - (2) Even if not apparent by history, at least a third of children with moderate to severe atopic dermatitis have IgE-mediated food allergies.
  - (3) Acute and chronic skin changes often coexist.
- 6. **Gastrointestinal syndromes:**
  - a. Oral allergy syndrome:
    - (1) Pollen-associated food allergy caused by cross-reactivity of antibodies to pollens (e.g., apple or tree pollen)
    - (2) Pruritus of oral mucosa after ingestion of certain fresh fruits and vegetables in patients with pollen allergies
    - (3) Rarely results in edema of oral mucosa
    - (4) Symptoms rarely progress beyond mouth
    - (5) Inciting antigens are destroyed by cooking
  - b. Allergic eosinophilic gastroenteritis, esophagitis:
    - (1) May cause abdominal pain, diarrhea, early satiety
    - (2) May be confused with reflux
    - (3) Characterized by eosinophilic infiltration of digestive tract
  - c. Food-induced enterocolitis:
    - (1) Presents in infancy
    - (2) Vomiting and diarrhea (may contain blood); when severe, may lead to lethargy, dehydration, hypotension, acidosis
    - (3) Most commonly associated with milk, soy
  - d. Infantile proctocolitis:
    - (1) Confined to distal colon and can present with diarrhea or blood-streaked and mucousy stools
    - (2) Symptoms usually resolve within 72 hours of stopping offending agent; rarely leads to anemia.
- 7. **Respiratory syndromes:**
  - a. Rhinitis (see [Section I](#))
  - b. Asthma (see Chapter 24)

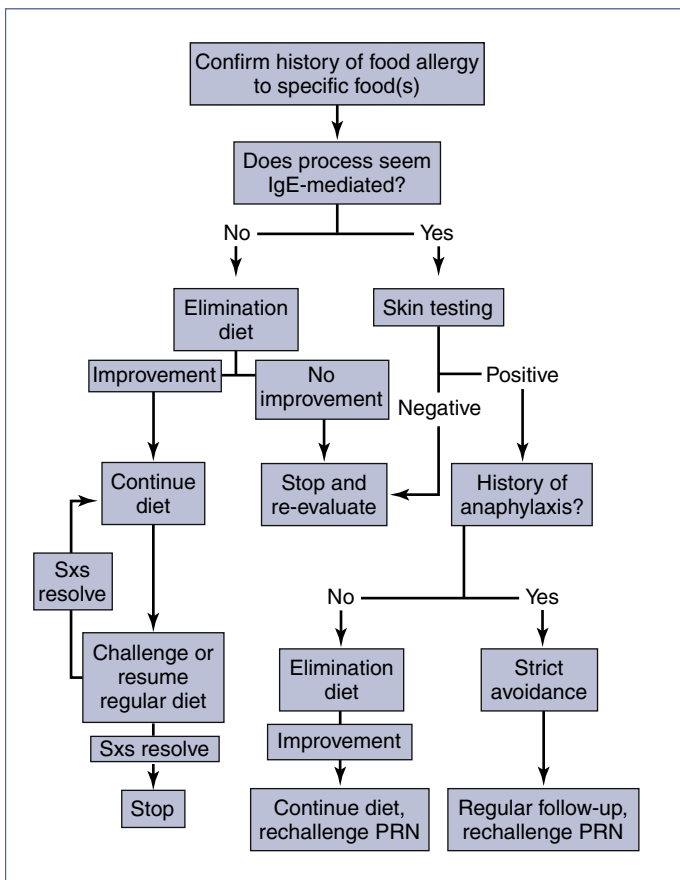
### C. Diagnosis of Food Allergy ([Fig. 15-1](#))

#### 1. History and physical examination:

- a. Identify specific foods and whether fresh vs. cooked.
- b. Establish timing and nature of reactions; patient should keep a food diary.
- c. Mainstays of diagnosis, but skin testing needed to identify trigger foods.

#### 2. Skin testing:

- a. Skin prick test has poor positive predictive value but very good negative predictive value.
- b. Patient must not be taking antihistamines.
- c. Widespread skin conditions (e.g., dermatographism, urticaria, severe eczema) may decrease accuracy.
- d. Intradermal tests have high false-positive rates and higher risk.
- e. Atopy patch testing (APT): Under investigation; no guidelines for use at this time.

**FIGURE 15-1**

Evaluation and management of food allergy. Sxs, Symptoms. (Data from Wood RA. *The natural history of food allergy*. Pediatrics. 2003;111:1631-1637; and Wood RA. *Up to Date* 2009. <http://www.uptodate.com>.)

### 3. Measurement of allergen-specific IgE:

- Like skin tests, has poor positive predictive value, excellent negative predictive value
- Commonly used antigens include milk, eggs, peanuts, tree nuts (e.g., cashew, walnut), soy, wheat
- Levels above a certain range (different for different antigens) have increasing positive predictive value
- Useful in patients with dermatologic conditions that preclude skin testing

e. IgE binding to specific allergen components currently in clinical use, enzyme assays based on anti-IgE antibodies

f. IgG testing not useful

**4. Oral food challenges:**

a. Can verify clinical reactivity to a specific food allergen

b. Must be done under close medical supervision with emergency medications readily available

c. Patient must not be taking antihistamines

d. Most effective when double-blinded using graded doses of disguised food

**5. Trial elimination diet:**

a. Helpful if improvement with removal of food from diet

b. May be used prior to oral food challenge to clear food from system

**D. Differential Diagnosis**

1. **Food intolerance:** Nonimmunologic, based on toxins or other properties of foods leading to adverse effects

**2. Malabsorption syndromes:**

a. Cystic fibrosis, celiac disease (see Chapter 12), lactase deficiency

b. Gastrointestinal (GI) malformations

**E. Treatment**

1. **Allergen avoidance** is the most important intervention for all types of food allergy.

a. Patients must pay close attention to food ingredients.

b. Infants with milk, soy allergies may be placed on elemental formula.

c. Nutritional counseling and regular growth monitoring are recommended.

**2. For angioedema, urticaria:**

a. Epinephrine is first-line treatment

b. Antihistamines, corticosteroids

c. Broad differential.

3. **Atopic dermatitis:** Symptomatic control (see Chapter 8)

4. **Anaphylaxis:** Epinephrine, all at-risk patients should have an epinephrine auto-injector.

5. **Food-specific immunotherapy** is under investigation; used to induce clinical desensitization to specific allergens.

**F. Natural History**

1. **About one third of allergies** are lost in a 1- to 2-year period (peanut, tree nut, and shellfish allergies rarely outgrown, however).

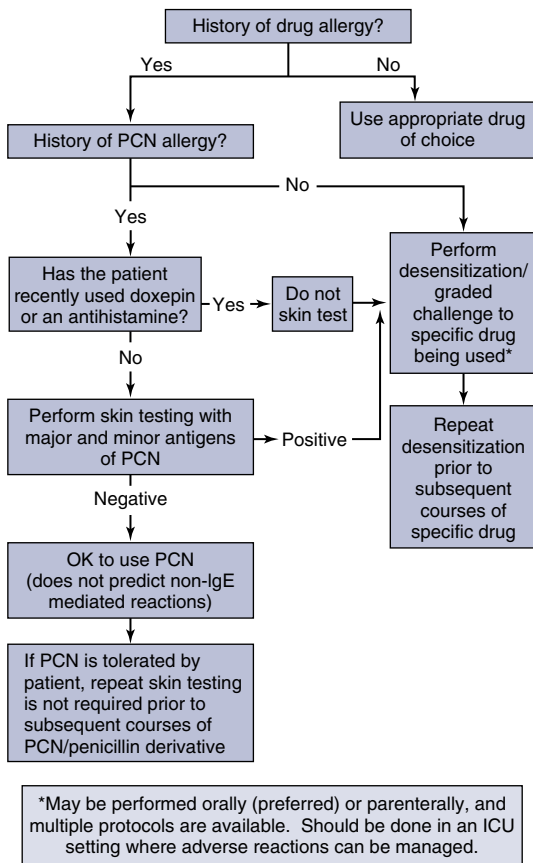
2. **Patients with prior anaphylaxis** also usually outgrow their food allergies.

3. **Skin tests and radioallergen sorbent testing (RAST)** may remain positive even though symptoms resolve.

**III. DRUG ALLERGY 10-11**

**A. Epidemiology**

1. **Drug allergy:** Immunologically mediated response to an agent in a sensitized person.

**FIGURE 15-2**

Evaluation and management of drug allergy. PCN, Penicillin. (Adapted from Solensky R. *Allergy to penicillins. Up to Date 2009.* <http://www.uptodate.com>.)

2. **Drug intolerance:** Undesirable pharmacologic effect.
3. **Although 10% of patients report penicillin allergy,** after evaluation, about 90% of individuals can tolerate penicillin.

## B. Diagnosis

1. **History:** Cutaneous manifestations are the most common presentation for drug allergic reactions.

## 2. Diagnostic studies:

- Penicillin is the only agent for which optimal negative predictive values for IgE-mediated reactions have been established.
- Skin testing with major and minor antigens of penicillin.

## C. Management (Fig. 15-2)

- Desensitization:** Immunologic IgE induction of tolerance, progressive administration of an allergenic substance to render effector cells less reactive
- Graded challenge:** Administration of progressively increasing doses of a drug until full dose is reached; does not modify a patient's response to the drug

## IV. EVALUATION OF SUSPECTED IMMUNODEFICIENCY

(TABLES 15-2 AND 15-3)<sup>12-19</sup>

## V. IMMUNOGLOBULIN THERAPY<sup>20-32</sup>

### A. Intravenous Immunoglobulin (IVIG)

#### 1. Indications:

- Replacement therapy for antibody-deficient disorders:
  - 400–500 mg/kg IV every 4 weeks to start.
  - Children with severe hypogammaglobulinemia (<100 mg/dL) may benefit from a total *loading* dose of 800 mg/kg given in two separate doses a few days apart, followed by 400–500 mg/kg every month.
  - Adjust dosing based on clinical response and to maintain trough IgG level of at least 500 mg/dL.
- Immune thrombocytopenic purpura:
  - Initially 400–2000 mg/kg (up to 1000 mg/kg given on a single day or in divided doses over 2–5 consecutive days).
  - Maintenance dose: 400–1000 mg/kg/dose every 3–6 weeks based on clinical response and platelet count.
  - May also use Rho(D) immune globulin (Win Rho) in Rh-positive patients.
- Kawasaki disease:
  - 2 g/kg × 1 dose over 8–12 hr.
  - If signs and symptoms persist, consider second dose of 2 g/kg.
  - Doses should be started within first 10 days of symptoms.
- Pediatric human immunodeficiency virus (HIV) infection with antibody deficiency (IgG concentration <400 mg/dL, failure to form antibodies to common antigens, recurrent serious bacterial infections, or measles prophylaxis): Dosing same as for antibody-deficient disorders mentioned previously.
- Bone marrow transplantation:
  - 400–500 mg/kg/dose to start; adjust dosing to maintain trough IgG level of at least 400 mg/dL
  - May decrease incidence of infection and death but not acute graft-versus-host disease
- Other potential uses:
  - Guillain-Barré syndrome
  - Refractory dermatomyositis and polymyositis
  - Chronic inflammatory demyelinating polyneuropathy

**TABLE 15-2**  
**WHEN TO SUSPECT IMMUNODEFICIENCY**

Recurrent Infections	Opportunistic Infections	Severe Infections	Other Conditions
6 or more new infections in 1 yr	<i>Pneumocystis jiroveci</i> pneumonia	2 or more months of antibiotics with little effect	Failure to gain weight or grow normally
Recurrent tissue or organ abscesses	<i>Pseudomonas</i> sepsis	Sepsis in the absence of a known risk (e.g., indwelling vascular catheter, neutropenia)	Family history of immunodeficiency or unexplained early deaths
2 or more serious sinus infections in 1 yr	Invasive infection with <i>Neisseria</i> spp.	Bacterial meningitis	Lymphopenia in infancy
2 or more pneumonias in 1 yr		Pneumonia with empyema	Complications from a live vaccine
		Resistant superficial or oral candidiasis	Part of a syndrome complex (e.g., Wiskott-Aldrich [with thrombocytopenia, eczema], DiGeorge syndrome [with facial dysmorphism, congenital cardiac disease, hypoparathyroidism])

Adapted from Stiehm ER. Approach to the child with recurrent infections. Up to Date 2009. <http://www.uptodate.com>.

**TABLE 15-3**  
**EVALUATION OF SUSPECTED IMMUNODEFICIENCY**

Suspected Functional Abnormality	Clinical Findings	Initial Tests	More-Advanced Tests
Antibody (e.g., common variable immunodeficiency, X-linked agammaglobulinemia, IgA deficiency)	Sinopulmonary and systemic infections (pyogenic bacteria) Enteric infections (enterovirus, other viruses, <i>Giardia</i> spp.) Autoimmune diseases (immune thrombocytopenia, hemolytic anemia, inflammatory bowel disease)	Immunoglobulin levels (IgG, IgM, IgA) Antibody levels to T-cell–dependent protein antigens (e.g., tetanus or pneumococcal conjugate vaccines) Antibody levels to T-cell–independent polysaccharide antigens in a child ≥2 yr (e.g., pneumococcal polysaccharide vaccine such as Pneumovax)	B-cell enumeration Immunofixation electrophoresis
Cell-mediated immunity (e.g., severe combined immunodeficiency, DiGeorge syndrome)	Pneumonia (pyogenic bacteria, fungi, <i>Pneumocystis jiroveci</i> , viruses)	Total lymphocyte counts HIV ELISA/Western blot/PCR	T-cell enumeration (CD3, CD4, CD8) In vitro T-cell proliferation to mitogens, antigens, or allogeneic cells FISH 22q11 for DiGeorge deletion

TABLE 15-3

## EVALUATION OF SUSPECTED IMMUNODEFICIENCY (Continued)

Suspected Functional Abnormality	Clinical Findings	Initial Tests	More-Advanced Tests
Phagocytosis (chronic granulomatous disease, leukocyte adhesion deficiency, Chédiak-Higashi syndrome)	Cutaneous infections, abscesses, lymphadenitis (staphylococci, enteric bacteria, fungi, mycobacteria), poor wound healing	WBC/neutrophil count and morphology	Nitroblue tetrazolium (NBT) test or dihydro-rhodamine (DHR) reduction test Chemotactic assay Phagocytic assay
Spleen	Bacteremia/hematogenous infection (pneumococcus, other streptococci, <i>Neisseria</i> spp.)	Peripheral blood smear for Howell-Jolly bodies Hemoglobin electrophoresis (HbSS)	Technetium-99 spleen scan or sonogram
Complement	Bacterial sepsis and other bloodborne infections (encapsulated bacteria, especially <i>Neisseria</i> spp.) Lupus, glomerulonephritis Angioedema	CH50 (total hemolytic complement)	Alternative pathway assay (AH50) Mannose-binding lectin level Individual complement component assays

ELISA, Enzyme-linked immunosorbent assay; FISH, fluorescent in situ hybridization; HIV, human immunodeficiency virus; PCR, polymerase chain reaction; WBC, white blood cell.

From Lederman HM. Clinical presentation of primary immunodeficiency diseases. In: McMillan J. *Oski's Pediatrics*. Philadelphia: Lippincott Williams & Wilkins; 2006:2441-2444.

## 2. Precautions and adverse reactions:

- Severe systemic symptoms (hemodynamic changes, respiratory difficulty, anaphylaxis).
- Less-severe systemic reactions (headache, myalgia, fever, chills, nausea, vomiting) may be alleviated by decreasing infusion rate or premedication with IV corticosteroids, antihistamines, and/or antipyretics.
- Aseptic meningitis syndrome.
- Acute renal failure (increased risk with preexisting renal insufficiency and with sucrose-containing IVIG).
- Acute venous thrombosis (increased risk with sucrose-containing IVIG).
- Use with caution in patients with undetectable IgA level due to trace amounts of IgA in IVIG (can lead to IgE-mediated anaphylaxis), although routine screening for IgA deficiency is not recommended in potential recipients.

## B. Intramuscular Immunoglobulin (IMIG)

### 1. Indications:

- Hepatitis A prophylaxis
- Measles prophylaxis
- Rubella prophylaxis



- d. Rabies prophylaxis
- e. Varicella-Zoster prophylaxis (independent of HIV status)

**2. Precautions and adverse reactions:**

- a. Severe systemic symptoms (hemodynamic changes, anaphylaxis).
- b. Local symptoms at injection site increase with repeated use; risk of local tissue injury.
- c. High risk for anaphylactoid reactions if given intravenously.
- d. Use with caution in patients with undetectable IgA levels, owing to trace amounts of IgA in IMIG.

**3. Dose of IMIG:**

- a. Hepatitis A postexposure prophylaxis: 0.02 mL/kg given within 14 days of exposure. Immunoglobulin is not needed if at least one dose of hepatitis A vaccine was given at  $\geq 1$  month before exposure.
- b. Measles prophylaxis: 0.25 mL/kg/dose (maximum dose 15 mL) given within 6 days of exposure in immunocompetent patient, and 0.5 mL/kg (maximum dose 15 mL) immediately following exposure in immunocompromised patients.
- c. Rubella prophylaxis during pregnancy: 0.55 mL/kg/dose within 72 hours of exposure.
- d. Rabies: 20 international units (IU)/kg single dose administered as soon as possible after exposure with the first dose of rabies vaccine.
- e. Varicella-zoster postexposure prophylaxis (independent of HIV status): (GamaSTAN™ S/D): 0.6-1.2 mL/kg/dose as a single dose within 72 hours of exposure

**4. Administration:**

- a. No more than 5 mL should be given at one site in an adult or large child.
- b. Smaller amounts per site (1-3 mL) for smaller children and infants.
- c. Administration of >15 mL at one time is essentially never warranted.
- d. Peak serum levels achieved by 48 hours; immune effect lasts 3-4 weeks.
- e. Intravenous or intradermal use of IMIG is absolutely contraindicated.

**C. Subcutaneous Immunoglobulin**

- 1. **Indication:** Replacement therapy for antibody deficiency.

**2. Dose:**

- a. 100-125 mg/kg weekly (maximum rate: 20 mL/hour; doses >15 mL usually should be divided between sites, but it depends on the amount of subcutaneous tissue).
- b. Larger doses can be given simultaneously in multiple sites or more frequently than once weekly.
- c. Using the same areas for injections improves tolerability.

- 3. **Precautions and adverse reactions:** similar to IMIG and IVIG; fewer systemic reactions because more slowly absorbed into circulation.

- 4. **Considerations:** does not require venous access or special nursing (parents can administer) but may require multiple needlesticks in larger children because of volume restriction per site.

## D. Specific Immunoglobulins

### 1. Hyperimmune globulins:

- Prepared from donors with high titers of specific antibodies
- Includes hepatitis B immune globulin (HBIG), varicella-zoster immune globulin (VZIG), cytomegalovirus immune globulin (CMV-IG), Rho(D) immune globulin, and others

### 2. Monoclonal antibody preparations (rituximab, palivizumab, and others)

## VI. IMMUNOLOGIC REFERENCE VALUES

### A. Serum IgG, IgM, IgA, and IgE Levels (Table 15-4)

### B. Serum IgG, IgM, IgA, and IgE Levels for Low Birth Weight Preterm Infants (Table 15-5)

### C. Serum IgG Subclass Levels (Table 15-6)

### D. Lymphocyte Enumeration (Table 15-7)

### E. Serum Complement Levels (Table 15-8)

TABLE 15-4

SERUM IMMUNOGLOBULIN LEVELS\*

Age	IgG (mg/dL)	IgM (mg/dL)	IgA (mg/dL)	IgE (IU/ml)
Cord blood (term)	1121 (636–1606)	13 (6.3–25)	2.3 (1.4–3.6)	0.22 (0.04–1.28)
1 mo	503 (251–906)	45 (20–87)	13 (1.3–53)	
6 wk				0.69 (0.08–6.12)
2 mo	365 (206–601)	46 (17–105)	15 (2.8–47)	
3 mo	334 (176–581)	49 (24–89)	17 (4.6–46)	0.82 (0.18–3.76)
4 mo	343 (196–558)	55 (27–101)	23 (4.4–73)	
5 mo	403 (172–814)	62 (33–108)	31 (8.1–84)	
6 mo	407 (215–704)	62 (35–102)	25 (8.1–68)	2.68 (0.44–16.3)
7–9 mo	475 (217–904)	80 (34–126)	36 (11–90)	2.36 (0.76–7.31)
10–12 mo	594 (294–1069)	82 (41–149)	40 (16–84)	
1 yr	679 (345–1213)	93 (43–173)	44 (14–106)	3.49 (0.80–15.2)
2 yr	685 (424–1051)	95 (48–168)	47 (14–123)	3.03 (0.31–29.5)
3 yr	728 (441–1135)	104 (47–200)	66 (22–159)	1.80 (0.19–16.9)
4–5 yr	780 (463–1236)	99 (43–196)	68 (25–154)	8.58 (1.07–68.9) <sup>†</sup>
6–8 yr	915 (633–1280)	107 (48–207)	90 (33–202)	12.89 (1.03–161.3) <sup>‡</sup>
9–10 yr	1007 (608–1572)	121 (52–242)	113 (45–236)	23.6 (0.98–570.6) <sup>§</sup>
14 yr				20.07 (2.06–195.2)
Adult	994 (639–1349)	156 (56–352)	171 (70–312)	13.2 (1.53–114)

\*Numbers in parentheses are the 95% confidence intervals (CIs).

<sup>†</sup>IgE data for 4 yr.

<sup>‡</sup>IgE data for 7 yr.

<sup>§</sup>IgE data for 10 yr.

From Kjellman NM, Johansson SG, Roth A. Serum IgE levels in healthy children quantified by a sandwich technique (PRIST). *Clin Allergy*. 1976;6:51-59; Jolliff CR, Cost KM, Stivins PC, et al. Reference intervals for serum IgG, IgA, IgM, C3, and C4 as determined by rate nephelometry. *Clin Chem*. 1982;28:126-128; and Zetterström O, Johansson SG. IgE concentrations measured by PRIST in serum of healthy adults and in patients with respiratory allergy: a diagnostic approach. *Allergy*. 1981;36:537-547.

**TABLE 15-5**

**SERUM IMMUNOGLOBULIN LEVELS FOR LOW BIRTH WEIGHT PRETERM INFANTS**

Age (mo)	Plasma IG Concentrations in 25- to 28-Wk Gestation Infants			Plasma IG Concentrations in 29- to 32-Wk Gestation Infants		
	IgG (mg/dL)*	IgM (mg/dL)*	IgA (mg/dL)*	IgG (mg/dL)*	IgM (mg/dL)*	IgA (mg/dL)*
0.25	251 (114–552) <sup>†</sup>	7.6 (1.3–43.3)	1.2 (0.07–20.8)	368 (186–728) <sup>†</sup>	9.1 (2.1–39.4)	0.6 (0.04–1.0)
0.5	202 (91–446)	14.1 (3.5–56.1)	3.1 (0.09–10.7)	275 (119–637)	13.9 (4.7–41)	0.9 (0.01–7.5)
1.0	158 (57–437)	12.7 (3.0–53.3)	4.5 (0.65–30.9)	209 (97–452)	14.4 (6.3–33)	1.9 (0.3–12.0)
1.5	134 (59–307)	16.2 (4.4–59.2)	4.3 (0.9–20.9)	156 (69–352)	15.4 (5.5–43.2)	2.2 (0.7–6.5)
2.0	89 (58–136)	16.0 (5.3–48.9)	4.1 (1.5–11.1)	123 (64–237)	15.2 (4.9–46.7)	3.0 (1.1–8.3)
3	60 (23–156)	13.8 (5.3–36.1)	3.0 (0.6–15.6)	104 (41–268)	16.3 (7.1–37.2)	3.6 (0.8–15.4)
4	82 (32–210)	22.2 (11.2–43.9)	6.8 (1.0–47.8)	128 (39–425)	26.5 (7.7–91.2)	9.8 (2.5–39.3)
6	159 (56–455)	41.3 (8.3–205)	9.7 (3.0–31.2)	179 (51–634)	29.3 (10.5–81.5)	12.3 (2.7–57.1)
8–10	273 (94–794)	41.8 (31.1–56.1)	9.5 (0.9–98.6)	280 (140–561)	34.7 (17–70.8)	20.9 (8.3–53)

\*Geometric mean.

<sup>†</sup>Numbers in parentheses are  $\pm 2$  SD.

From Ballow M, Cates KL, Rowe JC, et al. Development of the immune system in very low birth weight (less than 1500 g) premature infants: concentrations of plasma immunoglobulins and patterns of infections. *Pediatr Res*. 1986;9:899-904.

**TABLE 15-6**

**SERUM IgG SUBCLASS LEVELS\***

Age (yr)	IgG1 (mg/dL)	IgG2 (mg/dL)	IgG3 (mg/dL)	IgG4 (mg/dL)
0.5–1	290 (140–620)	58 (41–130)	41 (11–85)	0.2 (0–0.8)
1–1.5	350 (170–650)	62 (40–140)	42 (12–87)	3 (0–26)
1.5–2	400 (220–720)	80 (50–180)	44 (14–91)	7 (0–41)
2–3	450 (240–780)	95 (55–200)	46 (15–93)	14 (0–69)
3–4	480 (270–810)	115 (65–220)	48 (16–96)	20 (1–94)
4–6	500 (300–840)	130 (70–250)	50 (17–97)	26 (2–116)
6–9	570 (350–910)	170 (85–330)	54 (20–100)	37 (3–158)
9–12	600 (370–930)	210 (10–400)	58 (22–109)	47 (4–190)
12–18	580 (370–910)	260 (110–480)	63 (24–116)	49 (5–196)
Adult	500 (280–800)	300 (115–570)	64 (24–120)	35 (5–125)

\*Numbers in parentheses are the 95% confidence intervals (CIs).

From Schauer U, Stemberg F, Rieger CH, et al. IgG subclass concentrations in certified reference material 470 and reference values for children and adults determined with the binding site reagents. *Clin Chem*. 2003;49:1924-1929.

TABLE 15-7

## T AND B LYMPHOCYTES IN PERIPHERAL BLOOD

Age	CD3 (Total T cell) Count <sup>*,†</sup> (%) <sup>†</sup>	CD4 count <sup>*,†</sup> (%) <sup>†</sup>	CD8 Count <sup>*,†</sup> (%) <sup>†</sup>	CD19 (B cell) Count <sup>*,†</sup> (%) <sup>†</sup>
0–3 mo	2.50–5.50 (53–84)	1.60–4.00 (35–64)	0.56–1.70 (12–28)	0.30–2.00 (6–32)
3–6 mo	2.50–5.60 (51–77)	1.80–4.00 (35–56)	0.59–1.60 (12–23)	0.43–3.00 (11–41)
6–12 mo	1.90–5.90 (49–76)	1.40–4.30 (31–56)	0.50–1.70 (12–24)	0.61–2.60 (14–37)
1–2 yr	2.10–6.20 (53–75)	1.30–3.40 (32–51)	0.62–2.00 (14–30)	0.72–2.60 (16–35)
2–6 yr	1.40–3.70 (56–75)	0.70–2.20 (28–47)	0.49–1.30 (16–30)	0.39–1.40 (14–33)
6–12 yr	1.20–2.60 (60–76)	0.65–1.50 (31–47)	0.37–1.10 (18–35)	0.27–0.86 (13–27)
12–18 yr	1.00–2.20 (56–84)	0.53–1.30 (31–52)	0.33–0.92 (18–35)	0.11–0.57 (6–23)
Adult <sup>‡</sup>	0.70–2.10 (55–83)	0.30–1.40 (28–57)	0.20–0.90 (10–39)	

\*Absolute counts (number of cells per microliter  $\times 10^{-3}$ ).

†Normal values (10th to 90th percentile).

‡From Comans-Bitter WM, de Groot R, van den Beemd R, et al. Immunotyping of blood lymphocytes in childhood. Reference values for lymphocyte subpopulations. *J Pediatr*. 1997;130:388–393.

From Shearer WT, Rosenblatt HM, Gelman RS, et al. Lymphocyte subsets in healthy children from birth through 18 years of age: the Pediatric AIDS Clinical Trials Group P1009 study. *J Allergy Clin Immunol*. 2003;112:973–980.

TABLE 15-8

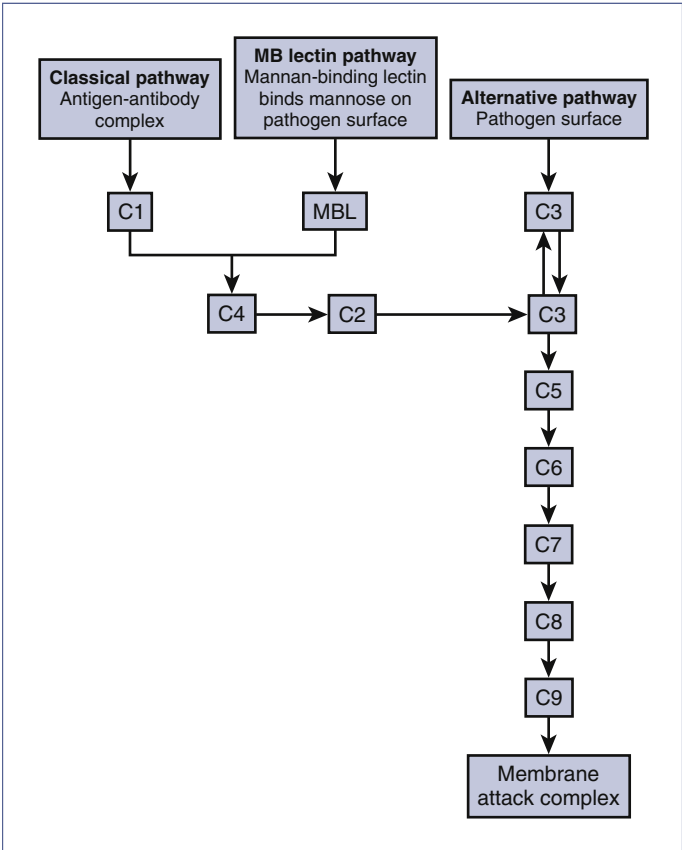
## SERUM COMPLEMENT LEVELS\*

Age	C3 (mg/dL)	C4 (mg/dL)
Cord blood (term)	83 (57–116)	13 (6.6–23)
1 mo	83 (53–124)	14 (7.0–25)
2 mo	96 (59–149)	15 (7.4–28)
3 mo	94 (64–131)	16 (8.7–27)
4 mo	107 (62–175)	19 (8.3–38)
5 mo	107 (64–167)	18 (7.1–36)
6 mo	115 (74–171)	21 (8.6–42)
7–9 mo	113 (75–166)	20 (9.5–37)
10–12 mo	126 (73–180)	22 (12–39)
1 yr	129 (84–174)	23 (12–40)
2 yr	120 (81–170)	19 (9.2–34)
3 yr	117 (77–171)	20 (9.7–36)
4–5 yr	121 (86–166)	21 (13–32)
6–8 yr	118 (88–155)	20 (12–32)
9–10 yr	134 (89–195)	22 (10–40)
Adult	125 (83–177)	28 (15–45)

\*Numbers in parentheses are the 95% confidence intervals (CIs).

Modified from Jolliff CR, Cost KM, Stivins PC, et al. Reference intervals for serum IgG, IgA, IgM, C3, and C4 as determined by rate nephelometry. *Clin Chem*. 1982;28:126–128.

VII. COMPLEMENT PATHWAY (FIG. 15-3)



**FIGURE 15-3**

Complement pathway. MB, Mannan-binding; MBL, mannan-binding lectin.

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# Chapter 16

## Immunoprophylaxis

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 See additional content on Expert Consult

### I. WEBSITES

American Academy of Pediatrics: *Red Book: 2012 Report of the Committee on Infectious Diseases*, 29th ed. 2012: <http://aapredbook.aappublications.org/>  
Food and Drug Administration: Vaccines Licensed for Immunization and Distribution in the US with Supporting Documents (including all package inserts): <http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/>  
Centers for Disease Control and Prevention: Vaccines and Immunization: Includes immunization schedules and *Morbidity and Mortality Weekly Reports* pertaining to vaccines: <http://www.cdc.gov/vaccines/>  
Centers for Disease Control and Prevention: Travelers' Health: <http://www.cdc.gov/travel/>  
Influenza vaccines A and B: [www.cdc.gov/flu/professionals/antivirals/index.htm](http://www.cdc.gov/flu/professionals/antivirals/index.htm)  
Vaccine Adverse Event Reporting System: <http://vaers.hhs.gov/index>  
World Health Organization: Vaccine, Blood, and Biologics: <http://www.who.int/immunization/en/>

### II. IMMUNIZATION SCHEDULES

Recommended Childhood Immunization Schedule (Fig. 16-1) and Catch-up Immunization Schedules, with minimum age for initial vaccination, minimum intervals between doses (Fig. 16-2), and accompanying footnotes (Fig. 16-3)<sup>1</sup>

### III. IMMUNIZATION GUIDELINES

#### A. Vaccine Informed Consent

Current forms for the vaccine information statement (VIS) can be obtained from the Centers for Disease Control and Prevention (CDC). The most recent VIS must be provided to the patient (non minor) or parent/guardian, with documentation of version date and date vaccine administered.

#### B. Vaccine Administration

##### 1. Preferred sites of administration of intramuscular (IM) and subcutaneous (SQ) vaccines:

- <18 months old: Anterolateral thigh
- Toddlers: Anterolateral thigh or deltoid (deltoid preferred if large enough)
- Adolescents and young adults: Deltoid

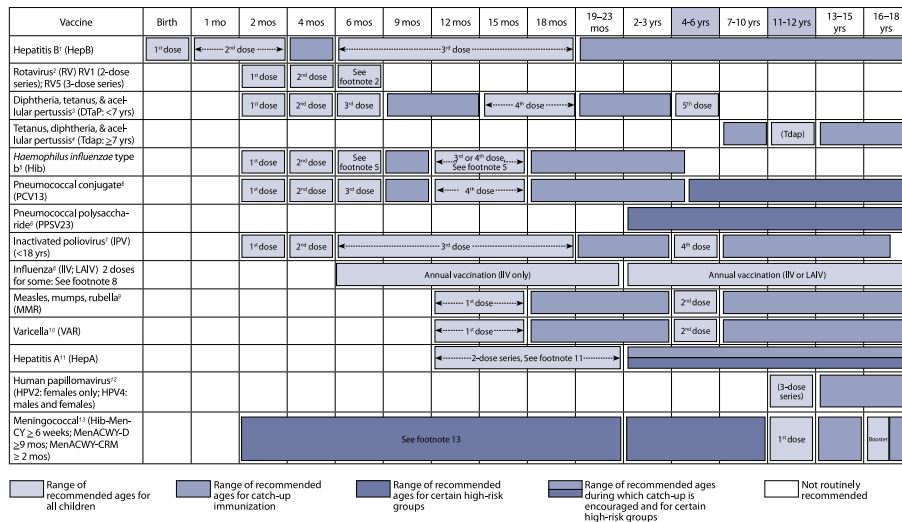
##### 2. Route:

- IM: Deep into muscle to avoid tissue damage from adjuvants, usually with a 22G–25G needle,  $\frac{7}{8}$  to 1 inch long in infants and toddlers, and 1 to 2 inches long in adolescents and young adults

Figure 1. Recommended immunization schedule for persons aged 0 through 18 years – United States, 2014.

(FOR THOSE WHO FALL BEHIND OR START LATE, SEE THE CATCH-UP SCHEDULE [FIGURE 2].)

These recommendations must be read with the footnotes that follow. For those who fall behind or start late, provide catch-up vaccination at the earliest opportunity as indicated by the green bars in Figure 1. To determine minimum intervals between doses, see the catch-up schedule (Figure 2). School entry and adolescent vaccine age groups are in bold.



This schedule includes recommendations in effect as of January 1, 2014. Any dose not administered at the recommended age should be administered at a subsequent visit, when indicated and feasible. The use of a combination vaccine generally is preferred over separate injections of its equivalent component vaccines. Vaccination providers should consult the relevant Advisory Committee on Immunization Practices (ACIP) statement for detailed recommendations, available online at <http://www.cdc.gov/vaccines/hcp/acip-recs/index.html>. Clinically significant adverse events that follow vaccination should be reported to the Vaccine Adverse Event Reporting System (VAERS) online (<http://www.vaers.hhs.gov>) or by telephone (800-822-7967). Suspected cases of vaccine-preventable diseases should be reported to the state or local health department. Additional information, including precautions and contraindications for vaccination, is available from CDC online (<http://www.cdc.gov/vaccines/recs/vac-admin/contraindications.html>) or by telephone (800-CDC-INFO [800-232-4636]). This schedule is approved by the Advisory Committee on Immunization Practices (<http://www.cdc.gov/vaccines/acip/>), the American Academy of Pediatrics (<http://www.aap.org>), the American Academy of Family Physicians (<http://www.aafp.org>), and the American College of Obstetricians and Gynecologists (<http://www.acog.org>).

**NOTE:** The above recommendations must be read along with the footnotes of this schedule.

## FIGURE 16-1

Recommended immunization schedule for persons aged 0–18 years—United States, 2013. (From ACIP Childhood/Adolescent Immunization Work Group: Advisory Committee on Immunization Practices [ACIP] recommended immunization schedule for persons aged 0 through 18 years—United States, 2013. MMWR Recomm Rep. 2013; 62:2-8. Available at [www.cdc.gov](http://www.cdc.gov).)



**FIGURE 2. Catch-up immunization schedule for persons aged 4 months through 18 years who start late or who are more than 1 month behind—United States, 2014.**

The figure below provides catch-up schedules and minimum intervals between doses for children whose vaccinations have been delayed. A vaccine series does not need to be restarted, regardless of the time that has elapsed between doses. Use the section appropriate for the child's age. Always use this table in conjunction with Figure 1 and the footnotes that follow.

Persons aged 4 months through 6 years					
Vaccine	Minimum Age for Dose 1	Minimum Interval Between Doses			
		Dose 1 to dose 2	Dose 2 to dose 3	Dose 3 to dose 4	Dose 4 to dose 5
Hepatitis B <sup>1</sup>	Birth	4 weeks	8 weeks and at least 16 weeks after first dose; minimum age for the final dose is 24 weeks		
Rotavirus <sup>2</sup>	6 weeks	4 weeks	4 weeks <sup>2</sup>		
Diphtheria, tetanus, & acellular pertussis <sup>3</sup>	6 weeks	4 weeks	4 weeks	6 months	6 months <sup>3</sup>
Haemophilus influenzae type b <sup>4</sup>	6 weeks	4 weeks if first dose administered at younger than age 12 months 8 weeks (as final dose) if first dose administered at age 12 through 14 months No further doses needed if first dose administered at age 15 months or older	4 weeks <sup>2</sup> if current age is younger than 12 months and first dose administered at < 7 months old 8 weeks and age 12 months through 59 months (as final dose) <sup>2</sup> if current age is younger than 12 months and first dose administered between 7 through 11 months (regardless of Hib vaccine [PRP-T or PRP-OMP] used for first dose); <b>Q2S</b> if current age is 12 through 59 months and first dose administered at younger than age 12 months; <b>Q2S</b> if first 2 doses were PRP-OMP and administered at younger than 12 months No further doses needed if previous dose administered at age 15 months or older	8 weeks (as final dose) This dose only necessary for children aged 12 through 59 months who received 3 (PRP-T) doses before age 12 months and started the primary series before age 7 months	
Pneumococcal <sup>5</sup>	6 weeks	4 weeks if first dose administered at younger than age 12 months 8 weeks (as final dose for healthy children) if first dose administered at age 12 months or older No further doses needed for healthy children if first dose administered at age 24 months or older	4 weeks if current age is younger than 12 months 6 weeks (as final dose for healthy children) if current age is 12 months or older No further doses needed for healthy children if previous dose administered at age 24 months or older	8 weeks (as final dose) This dose only necessary for children aged 12 through 59 months who received 3 doses before age 12 months or for children at high risk who received 3 doses at any age	
Inactivated poliovirus <sup>7</sup>	6 weeks	4 weeks <sup>7</sup>	4 weeks <sup>7</sup>	6 months <sup>7</sup> minimum age 4 years for final dose	
Meningococcal <sup>9</sup>	6 weeks	8 weeks <sup>11</sup>	See footnote 13	See footnote 13	
Measles, mumps, rubella <sup>8</sup>	12 months	4 weeks			
Varicella <sup>10</sup>	12 months	3 months			
Hepatitis A <sup>12</sup>	12 months	6 months			
Persons aged 7 through 18 years					
Tetanus, diphtheria, tetanus, diphtheria, & acellular pertussis <sup>3</sup>	7 years <sup>4</sup>	4 weeks	4 weeks if first dose of DTaP/DT administered at younger than age 12 months 6 months if first dose of DTaP/DT administered at age 12 months or older and then no further doses needed for catch-up	6 months if first dose of DTaP/DT administered at younger than age 12 months	
Human papillomavirus <sup>17</sup>	9 years		Routine dosing intervals are recommended <sup>19</sup>		
Hepatitis A <sup>12</sup>	12 months	6 months			
Hepatitis B <sup>1</sup>	Birth	4 weeks	8 weeks (and at least 16 weeks after first dose)		
Inactivated poliovirus <sup>7</sup>	6 weeks	4 weeks	4 weeks <sup>7</sup>	6 months <sup>7</sup>	
Meningococcal <sup>9</sup>	6 weeks	8 weeks <sup>11</sup>			
Measles, mumps, rubella <sup>8</sup>	12 months	4 weeks			
Varicella <sup>10</sup>	12 months	3 months if person is younger than age 13 years 4 weeks if person is aged 13 years or older			

**NOTE:** The above recommendations must be read along with the footnotes of this schedule.

**FIGURE 16-2**

Catch-up immunization schedule for persons aged 4 months–18 years who start late or who are more than 1 month behind—United States, 2013. (From ACIP Childhood/Adolescent Immunization Work Group: Advisory Committee on Immunization Practices [ACIP] recommended immunization schedule for persons aged 0 through 18 years—United States, 2013. MMWR Recomm Rep. 2013;62:2-8. Available at [www.cdc.gov/](http://www.cdc.gov/).)

## Footnotes — Recommended immunization schedule for persons aged 0 through 18 years—United States, 2014

For further guidance on the use of the vaccines mentioned below, see:

<http://www.cdc.gov/vaccines/hcp/acip-recs/index.html>.

For vaccine recommendations for persons 19 years of age and older, see the adult immunization schedule.

### Additional information

- For contraindications and precautions to use of a vaccine and for additional information regarding that vaccine, vaccination providers should consult the relevant ACIP statement available online at <http://www.cdc.gov/vaccines/acip-recs/index.html>.
- For purposes of calculating intervals between doses, 4 weeks = 28 days. Intervals of 4 months or greater are determined by calendar months.
- Vaccine doses administered 4 days or less before the minimum interval are considered valid. Doses of any vaccine administered  $\geq 5$  days earlier than the minimum interval or minimum age should not be counted as valid doses and should be repeated as age-appropriate. The repeat dose should be spaced after the invalid dose by the recommended minimum interval.
- For further details, see *MMWR, General Recommendations on Immunization and Reports / Vol. 60 / No. 2; Table 1. Recommended and minimum ages and intervals between vaccine doses* available online at <http://www.cdc.gov/mmwr/pdf/rr/r6002.pdf>.
- Information on travel vaccine requirements and recommendations is available at <http://wwwnc.cdc.gov/travel/destinations/list>.
- For vaccination of persons with primary and secondary immunodeficiencies, see Table 13, "Vaccination of persons with primary and secondary immunodeficiencies," in General Recommendations on Immunization (ACIP), available at <http://www.cdc.gov/mmwr/pdf/rr/r6002.pdf>; and American Academy of Pediatrics. Immunization in Special Clinical Circumstances, in Pickering LK, Baker CJ, Kimberlin DW, Long SS eds. *Red Book: 2012 report of the Committee on Infectious Diseases*. 29th ed. Elk Grove Village, IL: American Academy of Pediatrics.

### 1. Hepatitis B (HepB) vaccine. (Minimum age: birth)

#### Routine vaccination:

##### At birth:

- Administer monovalent HepB vaccine to all newborns before hospital discharge.
- For infants born to hepatitis B surface antigen (HBsAg)-positive mothers, administer HepB vaccine and 0.5 mL of hepatitis B immune globulin (HBIG) within 12 hours of birth. These infants should be tested for HBsAg and antibody to HBsAg (anti-HBs) 1 to 2 months after completion of the HepB series, at age 9 through 18 months (preferably at the next well-child visit).
- If mother's HBsAg status is unknown, within 12 hours of birth administer HepB vaccine regardless of birth weight. For infants weighing less than 2,000 grams, administer HBIG in addition to HepB vaccine within 12 hours of birth. Determine mother's HBsAg status as soon as possible and, if mother is HBsAg-positive, also administer HBIG for infants weighing 2,000 grams or more as soon as possible, but no later than age 7 days.

#### Doses following the birth dose:

- The second dose should be administered at age 1 or 2 months. Monovalent HepB vaccine should be used for doses administered before age 6 weeks.
- Infants who did not receive a birth dose should receive 3 doses of a HepB-containing vaccine on a schedule of 0, 1 to 2 months, and 6 months starting as soon as feasible. See Figure 2.
- Administer the second dose 1 to 2 months after the first dose (minimum intervals of 4 weeks), administer the third dose at least 8 weeks after the second dose AND at least 16 weeks after the first dose. The final (third or fourth) dose in the HepB vaccine series should be administered no earlier than age 24 weeks.
- Administration of a total of 4 doses of HepB vaccine is permitted when a combination vaccine containing HepB is administered after the birth dose.

#### Catch-up vaccination:

- Unvaccinated persons should complete a 3-dose series.
- A 2-dose series (doses separated by at least 4 months) of adult formulation Recombivax HB is licensed for use in children aged 11 through 15 years.
- For other catch-up guidance, see Figure 2.

### 2. Rotavirus (RV) vaccines. (Minimum age: 6 weeks for both RV1 [Rotarix] and RV5 [RotaTeq])

#### Routine vaccination:

Administer a series of RV vaccine to all infants as follows:

- If Rotarix is used, administer a 2-dose series at 2 and 4 months of age.
- If RotaTeq is used, administer a 3-dose series at ages 2, 4, and 6 months.
- If any dose in the series was RotaTeq or vaccine product is unknown for any dose in the series, a total of 3 doses of RV vaccine should be administered.

#### Catch-up vaccination:

- The maximum age for the first dose in the series is 14 weeks, 6 days; vaccination should not be initiated for infants aged 15 weeks, 0 days or older.
- The maximum age for the final dose in the series is 8 months, 0 days.
- For other catch-up guidance, see Figure 2.

For further guidance on the use of the vaccines mentioned below, see:  
<http://www.cdc.gov/vaccines/hcp/acip-recs/index.html>.

**3. Diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccine. (Minimum age: 6 weeks. Exception: DTaP-IPV [Kinrix]: 4 years)**

**Routine vaccination:**

- Administer a 5-dose series of DTaP vaccine at ages 2, 4, 6, 15 through 18 months, and 4 through 6 years. The fourth dose may be administered as early as age 12 months, provided at least 6 months have elapsed since the third dose.

**Catch-up vaccination:**

- The fifth dose of DTaP vaccine is not necessary if the fourth dose was administered at age 4 years or older.
- For other catch-up guidance, see Figure 2.

**4. Tetanus and diphtheria toxoids and acellular pertussis (Tdap) vaccine. (Minimum age: 10 years for Boostrix, 11 years for Adacel)**

**Routine vaccination:**

- Administer 1 dose of Tdap vaccine to all adolescents aged 11 through 12 years.
- Tdap may be administered regardless of the interval since the last tetanus and diphtheria toxoid-containing vaccine.
- Administer 1 dose of Tdap vaccine to pregnant adolescents during each pregnancy (preferred during 27 through 36 weeks gestation) regardless of time since prior Td or Tdap vaccination.

**Catch-up vaccination:**

- Persons aged 7 years and older who are not fully immunized with DTaP vaccine should receive Tdap vaccine as 1 (preferably the first dose in the catch-up series; additional doses are needed, use Td vaccine. For children 7 through 10 years who receive a dose of Tdap as part of the catch-up series, an adolescent Tdap vaccine dose at age 11 through 12 years should NOT be administered. Td should be administered instead 10 years after the Tdap dose.
- Persons aged 11 through 18 years who have not received Tdap vaccine should receive a dose followed by tetanus and diphtheria toxoids (Td) booster doses every 10 years thereafter.
- Inadvertent doses of DTaP vaccine:
  - If administered inadvertently to a child aged 7 through 10 years may count as part of the catch-up series. This dose may count as the adolescent Tdap dose, or the child can later receive a Tdap booster dose at age 11 through 12 years.
  - If administered inadvertently to an adolescent aged 11 through 18 years, the dose should be counted as the adolescent Tdap booster.
- For other catch-up guidance, see Figure 2.

**5. *Haemophilus influenzae* type b (Hib) conjugate vaccine. (Minimum age: 6 weeks for PRP-T [ACTHIB, DTaP-IPV/Hib (Pentacel) and Hib-MenCY (MenHibrix)], PRP-OMP [PedvaxHIB or COMVAX], 12 months for PRP-T [Hiberix])**

**Routine vaccination:**

- Administer a 2- or 3-dose Hib vaccine primary series and a booster dose (dose 3 or 4 depending on vaccine used in primary series) at age 12 through 15 months to complete a full Hib vaccine series.
- The primary series with ActHib, MenHibrix, or Pentacel consists of 3 doses and should be administered at 2, 4, and 6 months of age. The primary series with PedvaxHib or COMVAX consists of 2 doses and should be administered at 2 and 4 months of age; a dose at age 6 months is not indicated.
- One booster dose (dose 3 or 4 depending on vaccine used in primary series) of any Hib vaccine should be administered at age 12 through 15 months. An exception is Hiberix vaccine. Hiberix should only

**FIGURE 16-3—cont'd**

For further guidance on the use of the vaccines mentioned below, see:  
<http://www.cdc.gov/vaccines/hcp/acip-recs/index.html>.

##### 5. *Haemophilus influenzae* type b (Hib) conjugate vaccine (cont'd)

- For recommendations on the use of MenHibrix in patients at increased risk for meningococcal disease, please refer to the meningococcal vaccine footnotes and also to *MMWR* March 22, 2013; 62(RR02);1-22, available at <http://www.cdc.gov/mmwr/pdf/rr/r6202.pdf>.

###### Catch-up vaccination:

- If dose 1 was administered at ages 12 through 14 months, administer a second (final) dose at least 8 weeks after dose 1, regardless of Hib vaccine used in the primary series.
- If the first 2 doses were PRP-OMP (PedvaxHIB or COMVAX), and were administered at age 11 months or younger, the third (and final) dose should be administered at age 12 through 15 months and at least 8 weeks after the second dose.
- If the first dose was administered at age 7 through 11 months, administer the second dose at least 4 weeks later and a third (and final) dose at age 12 through 15 months or 8 weeks after second dose, whichever is later, regardless of Hib vaccine used for first dose.
- If first dose is administered at younger than 12 months of age and second dose is given between 12 through 14 months of age, a third (and final) dose should be given 8 weeks later.
- For unvaccinated children aged 15 months or older, administer only 1 dose.
- For other catch-up guidance, see Figure 2. For catch-up guidance related to MenHibrix, please see the meningococcal vaccine footnotes and also *MMWR* March 22, 2013; 62 (RR02);1-22, available at <http://www.cdc.gov/mmwr/pdf/rr/r6202.pdf>.

###### Vaccination of persons with high-risk conditions:

- Children aged 12 through 59 months who are at increased risk for Hib disease, including chemotherapy recipients and those with anatomic or functional asplenia (including sickle cell disease), human immunodeficiency virus (HIV) infection, immunoglobulin deficiency, or early component complement deficiency, who have received either no doses or only 1 dose of Hib vaccine before 12 months of age, should receive 2 additional doses of Hib vaccine 8 weeks apart; children who received 2 or more doses of Hib vaccine before 12 months of age should receive 1 additional dose.
  - For patients younger than 5 years of age undergoing chemotherapy or radiation treatment who received a Hib vaccine dose(s) within 14 days of starting therapy or during therapy, repeat the dose(s) at least 3 months following therapy completion.
  - Recipients of hematopoietic stem cell transplant (HSCT) should be revaccinated with a 3-dose regimen of Hib vaccine starting 6 to 12 months after successful transplant, regardless of vaccination history; doses should be administered at least 4 weeks apart.
  - A single dose of any Hib-containing vaccine should be administered to unimmunized\* children and adolescents 15 months of age and older undergoing an elective splenectomy; if possible, vaccine should be administered at least 14 days before procedure.
  - Hib vaccine is not routinely recommended for patients 5 years or older. However, 1 dose of Hib vaccine should be administered to unimmunized\* persons aged 5 years or older who have anatomic or functional asplenia (including sickle cell disease) and unvaccinated persons 5 through 18 years of age with human immunodeficiency virus (HIV) infection.
- \* Patients who have not received a primary series and booster dose or at least 1 dose of Hib vaccine after 14 months of age are considered unimmunized.

##### 6. Pneumococcal vaccines. (Minimum age: 6 weeks for PCV13, 2 years for PPSV23)

###### Routine vaccination with PCV13:

- Administer a 4-dose series of PCV13 vaccine at ages 2, 4, and 6 months and at age 12 through 15 months.
- For children aged 14 through 59 months who have received an age-appropriate series of 7-valent PCV (PCV7), administer a single supplemental dose of 13-valent PCV (PCV13).

###### Catch-up vaccination with PCV13:

- Administer 1 dose of PCV13 to all healthy children aged 24 through 59 months who are not completely vaccinated for their age.
- For other catch-up guidance, see Figure 2.

###### Vaccination of persons with high-risk conditions with PCV13 and PPSV23:

- All recommended PCV13 doses should be administered prior to PPSV23 vaccination if possible.
- For children 2 through 5 years of age with any of the following conditions: chronic heart disease (particularly cyanotic congenital heart disease and cardiac failure); chronic lung disease (including asthma if treated high-dose oral corticosteroid therapy); diabetes mellitus; cerebrospinal fluid leak; cochlear implant; sickle cell disease and other hemoglobinopathies; anatomic or functional asplenia; HIV infection; chronic renal failure; nephrotic syndrome; diseases associated with treatment with immunosuppressive drugs or radiation therapy, including malignant neoplasms, leukemias, lymphomas, and Hodgkin disease; solid organ transplantation; or congenital immunodeficiency:
  - Administer 1 dose of PCV13 if 3 doses of PCV (PCV7 and/or PCV13) were received previously.
  - Administer 2 doses of PCV13 at least 8 weeks apart if fewer than 3 doses of PCV (PCV7 and/or PCV13) were received previously.

For further guidance on the use of the vaccines mentioned below, see:  
<http://www.cdc.gov/vaccines/hcp/acip-recs/index.html>.

## 6. Pneumococcal vaccines (cont'd)

- 3. Administer 1 supplemental dose of PCV13 if 4 doses of PCV7 or other age-appropriate complete PCV7 series was received previously.
- 4. The minimum interval between doses of PCV (PCV7 or PCV13) is 8 weeks.
- 5. For children with no history of PPSV23 vaccination, administer PPSV23 at least 8 weeks after the most recent dose of PCV13.
- For children aged through 18 years who have cerebrospinal fluid leak; cochlear implant; sickle cell disease and other hemoglobinopathies; anatomic or functional asplenia; congenital or acquired immunodeficiencies; HIV infection; chronic renal failure; nephrotic syndrome; diseases associated with treatment with immunosuppressive drugs or radiation therapy, including malignant neoplasms, leukemias, lymphomas, and Hodgkin disease; generalized malignancy; solid organ transplantation; or multiple myeloma:
  1. If neither PCV13 nor PPSV23 has been received previously, administer 1 dose of PCV13 now and 1 dose of PPSV23 at least 8 weeks later.
  2. If PCV13 has been received previously but PPSV23 has not, administer 1 dose of PPSV23 at least 8 weeks after the most recent dose of PCV13.
  3. If PPSV23 has been received but PCV13 has not, administer 1 dose of PCV13 at least 8 weeks after the most recent dose of PPSV23.
- For children aged 6 through 18 years with chronic heart disease (particularly cyanotic congenital heart disease and cardiac failure), chronic lung disease (including asthma if treated with high-dose oral corticosteroid therapy), diabetes mellitus, alcoholism, or chronic liver disease, who have not received PPSV23, administer 1 dose of PPSV23. If PCV13 has been received previously, then PPSV23 should be administered at least 8 weeks after any prior PCV13 dose.
- A single revaccination with PPSV23 should be administered 5 years the first dose to children with sickle cell disease or other hemoglobinopathies; anatomic or functional asplenia; congenital or acquired immunodeficiencies; HIV infection; chronic renal failure; nephrotic syndrome; diseases associated with treatment with immunosuppressive drugs or radiation therapy, including malignant neoplasms, leukemias, lymphomas, and Hodgkin disease; generalized malignancy; solid organ transplantation; or multiple myeloma.

## 7. Inactivated poliovirus vaccine (IPV). (Minimum age: 6 weeks)

### Routine vaccination:

- Administer a 4-dose series of IPV at ages 2, 4, 6 through 18 months, and 4 through 6 years. The final dose in the series should be administered on or after the fourth birthday and at least 6 months after the previous dose.

### Catch-up vaccination:

- In the first 6 months of life, minimum age and minimum intervals are only recommended if the person is at risk for imminent exposure to circulating poliovirus (i.e., travel to a polio-endemic region or during an outbreak).
- If 4 or more doses are administered before age 4 years, an additional dose should be administered at age 4 through 6 years and at least 6 months after the previous dose.
- A fourth dose is not necessary if the third dose was administered at age 4 years or older and at least 6 months after the previous dose.
- If both OPV and IPV were administered as part of a series, a total of 4 doses should be administered, regardless of the child's current age. IPV is not routinely recommended for U.S. residents aged 18 years or older.
- For other catch-up guidance, see Figure 2.

## 8. Influenza vaccines. (Minimum age: 6 months for inactivated influenza vaccine [IIV], 2 years for live, attenuated influenza vaccine [LAIV])

### Routine vaccination

- Administer influenza vaccine annually to all children beginning at age 6 months. For most healthy, nonpregnant persons aged 2 through 49 years, either LAIV or IIV may be used. However, LAIV should NOT be administered to some persons, including 1) those with asthma, 2) children 2 through 4 years who NOT be administered to some persons, including 1) those with asthma, 2) children 2 through 4 years who had wheezing in the past 12 months, or 3) those who have any other underlying medical conditions that predispose them to influenza complications. For all other contraindications to use of LAIV, see *MMWR* 2013; 62 (No. RR-7):1-43, available at <http://www.cdc.gov/mmwr/pdf/rr/rr6207.pdf>.

### For children aged 6 months through 8 years:

- For the 2013–14 season, administer 2 doses (separated by at least 4 weeks) to children who are receiving influenza vaccine for the first time. Some children in this age group who have been vaccinated previously will also need 2 doses. For additional guidance, follow dosing guidelines in the 2013–14 ACIP influenza vaccine recommendations, *MMWR* 2013; 62 (No. RR-7):1-43, available at <http://www.cdc.gov/mmwr/pdf/rr/rr6207.pdf>.
- For the 2014–15 season, follow dosing guidelines in the 2014 ACIP influenza vaccine recommendations.

### For persons aged 9 years and older:

- Administer 1 dose.

For further guidance on the use of the vaccines mentioned below, see:  
<http://www.cdc.gov/vaccines/hcp/acip-recs/index.html>.

**9. Measles, mumps, and rubella (MMR) vaccine. (Minimum age: 12 months for routine vaccination)**

**Routine vaccination:**

- Administer a 2-dose series of MMR vaccine at ages 12 through 15 months and 4 through 6 years. The second dose may be administered before age 4 years, provided at least 4 weeks have elapsed since the first dose.
- Administer 1 dose of MMR vaccine to infants aged 6 through 11 months before departure from the United States for international travel. These children should be revaccinated with 2 doses of MMR vaccine, the first at age 12 through 15 months (12 months if the child remains in an area where disease risk is high), and the second dose at least 4 weeks later.
- Administer 2 doses of MMR vaccine to children aged 12 months and older before departure from the United States for international travel. The first dose should be administered on or after age 12 months and the second dose at least 4 weeks later.

**Catch-up vaccination:**

- Ensure that all school-aged children and adolescents have had 2 doses of MMR vaccine; the minimum interval between the 2 doses is 4 weeks.

**10. Varicella (VAR) vaccine. (Minimum age: 12 months)**

**Routine vaccination:**

- Administer a 2-dose series of VAR vaccine at ages 12 through 15 months and 4 through 6 years. The second dose may be administered before age 4 years, provided at least 3 months have elapsed since the first dose. If the second dose was administered at least 4 weeks after the first dose, it can be accepted as valid.

**Catch-up vaccination:**

- Ensure that all persons aged 7 through 18 years without evidence of immunity (see *MMWR* 2007; 56 [No. RR-4], available at <http://www.cdc.gov/mmwr/pdf/rr/r5604.pdf>) have 2 doses of varicella vaccine. For children aged 7 through 12 years, the recommended minimum interval between doses is 3 months (if the second dose was administered at least 4 weeks after the first dose, it can be accepted as valid); for persons aged 13 years and older, the minimum interval between doses is 4 weeks.

**11. Hepatitis A (HepA) vaccine. (Minimum age: 12 months)**

**Routine vaccination:**

- Initiate the 2-dose HepA vaccine series at 12 through 23 months; separate the 2 doses by 6 to 18 months.
- Children who have received 1 dose of HepA vaccine before age 24 months should receive a second dose 6 to 18 months after the first dose.
- For any person aged 2 years and older who has not already received the HepA vaccine series, 2 doses of HepA vaccine separated by 6 to 18 months may be administered if immunity against hepatitis A virus infection is desired.

**Catch-up vaccination:**

- The minimum interval between the two doses is 6 months.

**Special populations:**

- Administer 2 doses of HepA vaccine at least 6 months apart to previously unvaccinated persons who live in areas where vaccination programs target older children, or who are at increased risk for infection. This includes persons traveling to or working in countries that have high or intermediate endemicity of infection; men having sex with men; users of injection and non-injection illicit drugs; persons who work with HAV-infected primates or with HAV in a research laboratory; persons with clotting-factor disorders; persons with chronic liver disease; and persons who anticipate close, personal contact (e.g., household or regular babysitting) with an international adoptee during the first 60 days after arrival in the United States from a country with high or intermediate endemicity. The first dose should be administered as soon as the adoption is planned, ideally 2 or more weeks before the arrival of the adoptee.

**12. Human papillomavirus (HPV) vaccines. (Minimum age: 9 years for HPV2 [Cervarix] and HPV4 [Gardasil])**

**Routine vaccination:**

- Administer a 3-dose series of HPV vaccine on a schedule of 0, 1-2, and 6 months to all adolescents aged 11 through 12 years. Either HPV4 or HPV2 may be used for females, and only HPV4 may be used for males.
- The vaccine series may be started at age 9 years.
- Administer the second dose 1 to 2 months after the first dose (minimum interval of 4 weeks), administer the third dose 24 weeks after the first dose and 16 weeks after the second dose (minimum interval of 12 weeks).

**Catch-up vaccination:**

- Administer the vaccine series to females (either HPV2 or HPV4) and males (HPV4) at age 13 through 18 years if not previously vaccinated.
- Use recommended routine dosing intervals (see above) for vaccine series catch-up.

For further guidance on the use of the vaccines mentioned below, see:  
<http://www.cdc.gov/vaccines/hcp/acip-recs/index.html>.

**13. Meningococcal conjugate vaccines. (Minimum age: 6 weeks for Hib-MenCY [MenHibrix], 9 months for MenACWY-D [Menactra], 2 months for MenACWY-CRM [Menveo])**

**Routine vaccination:**

- Administer a single dose of Menactra or Menveo vaccine at age 11 through 12 years, with a booster dose at age 16 years.
- Adolescents aged 11 through 18 years with human immunodeficiency virus (HIV) infection should receive a 2-dose primary series of Menactra or Menveo with at least 8 weeks between doses.
- For children aged 2 months through 18 years with high-risk conditions, see below.

**Catch-up vaccination:**

- Administer Menactra or Menveo vaccine at age 13 through 18 years if not previously vaccinated.
- If the first dose is administered at age 13 through 15 years, a booster dose should be administered at age 16 through 18 years with a minimum interval of at least 8 weeks between doses.
- If the first dose is administered at age 16 years or older, a booster dose is not needed.
- For other catch-up guidance, see Figure 2.

**Vaccination of persons with high-risk conditions and other persons at increased risk of disease:**

- Children with anatomic or functional asplenia (including sickle cell disease):
  1. For children younger than 19 months of age, administer a 4-dose infant series of MenHibrix or Menveo at 2, 4, 6, and 12 through 15 months of age.
  2. For children aged 19 through 23 months who have not completed a series of MenHibrix or Menveo, administer 2 primary doses of Menveo at least 3 months apart.
  3. For children aged 24 months and older who have not received a complete series of MenHibrix or Menveo or Menactra, administer 2 primary doses of either Menactra or Menveo at least 2 months apart. If Menactra is administered to a child with asplenia (including sickle cell disease), do not administer Menactra until 2 years of age and at least 4 weeks after the completion of all PCV13 doses.
- Children with persistent complement component deficiency
  1. For children younger than 19 months of age, administer a 4-dose infant series of either MenHibrix or Menveo at 2, 4, 6, and 12 through 15 months of age.
  2. For children 7 through 23 months who have not initiated vaccination, two options exist depending on age and vaccine brand:
    - a. For children who initiate vaccination with Menveo at 7 months through 23 months of age, a 2-dose series should be administered with the second dose after 12 months of age and at least 3 months after the first dose.
    - b. For children who initiate vaccination with Menactra at 9 months through 23 months of age, a 2-dose series of Menactra should be administered at least 3 months apart.
    - c. For children aged 24 months and older who have not received a complete series of MenHibrix, Menveo, or Menactra, administer 2 primary doses of either Menactra or Menveo at least 2 months apart.
- For children who travel to or reside in countries in which meningococcal disease is hyperendemic or epidemic, including countries in the African meningitis belt or the Hajj, administer an age-appropriate formulation and series of Menactra or Menveo for protection against serogroups A and W meningococcal disease. Prior receipt of MenHibrix is not sufficient for children traveling to the meningitis belt or the Hajj because it does not contain serogroups A or W.
- For children at risk during a community outbreak attributable to a vaccine serogroup, administer or complete an age- and formulation-appropriate series of MenHibrix, Menactra, or Menveo.
- For booster doses among persons with high-risk conditions, refer to *MMWR* 2013; 62 (RR02);1-22, available at <http://www.cdc.gov/mmwr/preview/mmwrhtml/r6202a1.htm>.

**Catch-up recommendations for persons with high-risk conditions:**

1. If MenHibrix is administered to achieve protection against meningococcal disease, a complete age-appropriate series of MenHibrix should be administered.
2. If the first dose of MenHibrix is given at or after 12 months of age, a total of 2 doses should be given at least 8 weeks apart to ensure protection against serogroups C and Y meningococcal disease.
3. For children who initiate vaccination with Menveo at 7 months through 9 months of age, a 2-dose series should be administered with the second dose after 12 months of age and at least 3 months after the first dose.
4. For other catch-up recommendations for these persons, refer to *MMWR* 2013; 62 (RR02);1-22, available at <http://www.cdc.gov/mmwr/preview/mmwrhtml/r6202a1.htm>.

**For complete information on use of meningococcal vaccines, including guidance related to vaccination of persons at increased risk of infection, see *MMWR* March 22, 2013; 62 (RR02);1-22, available at <http://www.cdc.gov/mmwr/pdf/rr/r6202a1.pdf>.**

**FIGURE 16-3**

Footnotes: Recommended immunization schedule for persons aged 0 through 18 years—United States, 2013. (From *ACIP Childhood/Adolescent Immunization Work Group: Advisory Committee on Immunization Practices [ACIP] recommended immunization schedule for persons aged 0 through 18 years—United States, 2013*. *MMWR Recomm Rep*. 2013;62:2-8. Available at [www.cdc.gov](http://www.cdc.gov).)

b. SQ: Into pinched skin fold with a 23G–25G,  $\frac{5}{8}$ - to  $\frac{3}{4}$ -inch needle

### 3. **Simultaneous administration:**

- a. Routine childhood vaccines are safe and effective when administered simultaneously at different sites, generally 1–2 inches apart. This includes inactivated and live vaccines.
- b. If live vaccines are not given at the same visit, an interval of 28 days should be allotted between them.

## C. Vaccine Types

1. **Live vaccines:** Influenza (intranasal); measles, mumps, and rubella (MMR); polio (oral); rotavirus; tuberculosis (BCG); typhoid (oral); varicella; yellow fever
2. **Nonlive vaccines:** Diphtheria, tetanus, pertussis combination vaccines (DTaP/DT/Td/Tdap), hepatitis A (HepA), hepatitis B (HepB), *Haemophilus influenzae* type b (Hib), human papillomavirus (HPV), influenza (injectable), Japanese encephalitis, meningococcal, pneumococcal, rabies, typhoid (injectable)

## D. Misconceptions

1. Misconceptions about the need for and safety of recommended immunizations have been associated with underimmunization and/or delay in immunization.
2. The CDC and American Academy of Pediatrics (AAP) publish Provider Resources for Vaccine Conversations with Parents, available at <http://www.cdc.gov/vaccines/hcp/patient-ed/conversations/index.html>, for up-to-date vaccine information and resources to effectively communicate with parents regarding vaccines.

## E. General Indications and Precautions for All Vaccines

This information is based on the Advisory Committee on Immunization Practices (ACIP) and the Committee on Infectious Diseases from the AAP and may vary from those listed on the manufacturers' inserts<sup>2</sup>:

1. **Contraindications** (vaccines should not be given):
  - a. Anaphylactic reaction to a vaccine or a vaccine constituent contraindicates further doses of that vaccine or vaccines containing that substance (e.g., streptomycin and neomycin).
2. **Precautions:** If risks are believed to outweigh benefits, immunization should be withheld; if benefits are believed to outweigh risks (e.g., to complete primary series, during an outbreak, or foreign travel, immunization should be given)
  - a. Moderate or severe illnesses with or without a fever
  - b. Anaphylactic latex allergy (vaccines supplied in vials or syringes that contain natural rubber, a list is available from the CDC at <http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/B/latex-table.pdf>)
3. **Misconceptions:** Vaccines should be given in the circumstances below, as well as those listed in the specific vaccine sections:
  - a. Mild to moderate local reaction (soreness, redness, swelling) after a dose of an injectable antigen; low-grade or moderate fever after a previous vaccine dose



- b. Nonanaphylactic latex allergies (e.g., contact allergy to latex gloves)
- c. Mild acute illness with or without low-grade fever, current antimicrobial therapy, or convalescent phase of illnesses
- d. Malnutrition
- e. Family history of adverse event to immunization
- f. History of penicillin or other nonspecific allergies
- g. Unimmunized or immunodeficient household contact (exception is live attenuated influenza virus [LAIV], which should not be administered to close contacts of persons with severe immunosuppression)
- h. Pregnancy of mother or household contact
- i. Breast-feeding (nursing infant *OR* lactating mother). Exception: yellow fever vaccine, which is a precaution.

#### IV. IMMUNOPROPHYLAXIS GUIDELINES FOR SPECIAL HOSTS

##### A. Children at High Risk for Pneumococcal Disease

###### 1. Definition:

- a. Immunocompetent children: Those with chronic heart disease, chronic lung disease, diabetes mellitus, cerebrospinal fluid (CSF) leaks, cochlear implants
  - b. Immunocompromised children: Those with asplenia (functional or anatomic), human immunodeficiency virus (HIV), chronic renal failure or nephrotic syndrome, malignancy, immunosuppressive therapy, congenital immunodeficiency
2. **For those <6 years of age**, complete primary series with PCV13 (pneumococcal conjugate vaccine).
  3. **For those >6 years of age** and not fully immunized, give 1 dose of PCV13, no matter how many prior doses previously received.
  4. Give 1 dose of 23PS (23-valent pneumococcal polysaccharide vaccine)  $\geq 8$  weeks after last dose of PCV13 if  $\geq 2$  years of age.
  5. **For Immunocompromised children:** A single booster of 23PS is indicated after 5 years of age but should not be repeated.<sup>3</sup>

##### B. Children at High Risk for Meningococcal Disease

1. **Definition:** Those with asplenia (functional or anatomic) or persistent complement deficiency.
2. **If <19 months**, give Hib MenCY or MenACWY-CRM vaccine series.
3. **If 9–23 months** and have persistent complement deficiency, can alternatively give meningococcal conjugate vaccine MenACWY-D series.
4. **When  $\geq 2$  years**, give either MenACWY series. Boosters of MenACWY should be given every 5 years in this group. For travelers to countries in the “meningitis belt” or the Hajj, children should receive protection against groups A and W-135 with MCV4 doses if  $\geq$  age 9 months, and receive boosters every 3 years (children aged 2–6 years) or 5 years (children  $>$  age 6).

##### C. Children at High Risk for Hib Disease

1. **Definition:** Those with immunocompromising conditions including cancers, anatomic or functional asplenia, and HIV.
2. **If <12 months**, give primary series.

3. **If 12–59 months** and have received only 1 dose, should receive 2 additional doses separated by 8 weeks. If 2 doses received before 12 months, should receive a third dose.
4. **If >5 years** and unimmunized, should receive 1 dose.

#### D. Functional or Anatomic Asplenia (Including Sickle Cell Disease)

1. **Penicillin prophylaxis:** See Chapter 14.
2. **Pneumococcal vaccines:** See [Section IV.A](#).
3. **Meningococcal vaccines:** See [Section IV.B](#).
4. **Hib vaccines:** See [Section IV.C](#).
5. **Children ≥2 years** undergoing elective splenectomy should ideally receive pneumococcal and MCV vaccines at least 2 weeks before surgery for optimal immune response and may also benefit from another dose of Hib

#### E. Congenital Immunodeficiency Disorders

1. **Live vaccines are generally contraindicated.** See Table 1.16 in the *AAP Red Book*<sup>2</sup> for details regarding individual immunodeficiencies.
2. **Inactivated vaccines should be given** according to the routine schedule. Immune response may vary and may be inadequate; titers can be used to assess response.
3. **Immunoglobulin (Ig) therapy** may be indicated.
4. **Household contacts:** Immunize according to routine immunization schedule.

#### F. Known or Suspected HIV Disease

1. **Inactivated vaccines should be given** according to the routine immunization schedule. Influenza vaccine should be given yearly.
  - a. Pneumococcal vaccines: See [Section IV.A](#)
  - b. Meningococcal vaccines: Administer 2 doses at least 8 weeks apart starting at age 11 years
  - c. Hib vaccines: See [Section IV.C](#)
2. **Live vaccines:**
  - a. MMR and varicella vaccines should be given to asymptomatic or mildly symptomatic patients with CD4 cell count of 15% or greater.<sup>4</sup> Do not administer the measles, mumps, rubella, and varicella (MMRV) combination vaccine.
  - b. Do not administer LAIV. Oral (live attenuated) poliovirus (OPV) and BCG vaccine are generally not given except in areas where risk of disease is thought to outweigh possibility of vaccine-associated disease.
3. **Passive immunoprophylaxis or chemoprophylaxis should be considered** after exposures.

#### G. Oncology Patients

(See [Table 16-1](#) for general guidelines.)

1. **During active chemotherapy,** immune response to vaccines may be less than ideal. Titers may be useful to assess response.
2. **All live vaccines** should be delayed at least 3 months after immunosuppressive therapy has been discontinued.
3. **Hematopoietic stem cell transplant recipients:** Will need reimmunization against vaccine-preventable illnesses after their transplantation. See

**TABLE 16-1**  
**IMMUNIZATION FOR GENERAL ONCOLOGY PATIENTS**

Vaccine	Indications and Comments
DTaP/Tdap, Hib, HBV, IPV	Indicated for incompletely immunized children
PCV13, 23PS	Indicated for incompletely immunized children (see <a href="#">Section IV.A</a> )
Meningococcal	Consider in asplenic patients (see <a href="#">Section IV.B</a> )
Influenza	Defer in active chemotherapy; may give as early as 3–4 wk after remission and off chemotherapy if during influenza season; peripheral granulocyte and lymphocyte counts should be >1000/ $\mu$ L; should be given to household contacts
MMR	Contraindicated until child is in remission and finished with all chemotherapy for 3–6 mo; may need reimmunization after chemotherapy if titers have fallen below protective levels
Varicella	Consider immunizing children who have remained in remission and have finished chemotherapy for >1 yr; with absolute lymphocyte count of >700/ $\mu$ L and platelet count of >100,000/ $\mu$ L within 24 hr of immunization; check titers of previously immunized children to verify protective levels of antibodies

Data from American Academy of Pediatrics. *Red Book: 2012 Report of the Committee on Infectious Diseases*. 29th ed. Elk Grove Village, Ill: AAP, 2012.

[Table EC 16-A](#) for guidelines regarding when vaccination can be reinitiated after transplantation.

**H. Patients with Solid Organ Transplants**

Administer live vaccines at least a month before transplant. Ensure all other vaccines are up to date. Safety and efficacy of inactivated vaccines after transplant are still unclear; they are generally given as scheduled after 6 months post transplant, when immunosuppression is less intense.

**I. Patients on Corticosteroids**

Only live vaccines are potentially contraindicated (see [Table 16-2](#) for details).

**TABLE 16-2**  
**LIVE VACCINE IMMUNIZATION FOR PATIENTS RECEIVING CORTICOSTEROID THERAPY**

Steroid Dose	Recommended Guidelines
Topical, inhaled, or local injection of steroids	Live vaccines can generally be given; if there is clinical evidence of immunosuppression, wait 1 mo after cessation of therapy.
Low-dose steroids (<2 mg/kg/day or <20 mg/day of prednisone equivalent), including physiologic doses	Live vaccines may be given.
High-dose steroids ( $\geq 2$ mg/kg/day or $\geq 20$ mg/day of prednisone equivalent)	
Duration of therapy < 14 days	May give live vaccines immediately after cessation of therapy (but consider 2-wk delay in administration).
Duration of therapy $\geq 14$ days	Do not give live vaccines until therapy has been discontinued for 1 mo.

Modified from American Academy of Pediatrics. *Red Book: 2012 Report of the Committee on Infectious Diseases*. 29th ed. Elk Grove Village, Ill: AAP, 2012.

TABLE EC 16-A

## IMMUNIZATION FOR HEMATOPOIETIC STEM CELL TRANSPLANT RECIPIENTS

Vaccines	Months After Transplant	Instructions
PCV13 and PS23	3–6	3 doses of PCV13. If no chronic graft-vs-host disease (GVHD) at 12 mo after transplant and $\geq 2$ years of age, give PS23. For patients with chronic GVHD, give a fourth dose of PCV13.
Influenza	4–6	Give annually. A second dose is needed the first season ( $\geq 4$ weeks after the first).
DTaP	6	If $> 7$ years give 3 doses of DTaP. If $\geq 7$ years, give 1 dose of Tdap and 2 doses of tetanus-diphtheria (Td) vaccine. If have tetanus-prone wound, give tetanus immune globulin (TIG) during first year after transplantation.
HepB	6–12	3 doses. Postimmunization serologic testing may be considered after completion of series. Additional doses of vaccine (maximum of 3) may be given to vaccine nonresponders.
Hib	6–12	3 doses
MCV	6–12	1 dose
IPV	6–12	3 doses
HepA	12	2 doses. Consider for patients with chronic liver disease, chronic GVHD, or travelers to areas with endemic disease.
Measles	$\geq 24$	2 doses for children OR 1 dose for adolescents and adults. Consider in those seronegative to measles without chronic GVHD or ongoing immunosuppression.
Varicella	$\geq 24$	2 doses for children OR 1 dose for adolescents and adults. Consider in those seronegative to varicella without chronic GVHD or ongoing immunosuppression.

Data from American Academy of Pediatrics. *Red Book: 2012 Report of the Committee on Infectious Diseases*. 29th ed. Elk Grove Village, Ill: AAP, 2012.

**J. Patients on Biological Response Modifier Therapy (Cytokine Inhibitors)**

Administer live vaccines a minimum of 4 weeks before initiating therapy. Ensure all other vaccines are up to date. Vaccine efficacy unclear while on therapy.

**K. Pregnancy**

1. **Give Tdap during each pregnancy** (preferred during 27th–36th wk of gestation), regardless of prior immunization status. Generally inactivated influenza vaccine is also strongly recommended.
2. Other inactivated vaccines are considered precautionary and generally deferred until after the pregnancy.
3. **Live vaccines** are generally contraindicated during pregnancy. The only exception is yellow fever, which is precautionary and should be given if the risk of yellow fever is high when travelling.

**L. Preterm and Low-Birth-Weight Infants**

1. **Immunize according to chronologic age, using regular vaccine dosage.**
2. **HepB:** Initiation of HepB vaccine may be delayed for infants of hepatitis B surface antigen (HBsAg)-negative mothers until the child is >2 kg or age 2 months, whichever is earlier. See Fig. 16-4 for management of preterm infant born to mother with HepB.

**M. Patients Treated with Immunoglobulin or Other Blood Products**

See Table EC 16-B for suggested intervals between any immunoglobulin or blood product administration (including packed red blood cells [pRBCs]) and MMR or varicella immunization. This time allows decrease in passive antibodies so children will have an adequate response to the vaccine, but they should not be considered adequately protected after product administrations. Blood products and immunoglobulin are not thought to interfere with non-measles or varicella vaccines.

**N. Travelers to Foreign Countries**

See CDC's Travel Health page on vaccinations (available at <http://www.cdc.gov/travel/page/vaccinations.htm>) for specific recommendations on vaccines by destination. If assistance in obtaining appropriate vaccines for a patient/referral to a travel clinic is indicated, authorized U.S. yellow fever vaccination clinics are generally good options (searchable at <http://www.cdc.gov/travel/yellow-fever-vaccination-clinics/search.htm>).

**V. IMMUNOPROPHYLAXIS GUIDELINES FOR SPECIFIC DISEASES****A. Diphtheria/Tetanus/Pertussis Vaccines and Tetanus Immunoprophylaxis****1. Description:**

- a. DTaP: Diphtheria and tetanus toxoids combined with acellular pertussis vaccine; preferred formulation for children <7 years of age.
- b. DT: Diphtheria and tetanus toxoids without pertussis vaccine; use in children <7 years of age in whom pertussis vaccine is contraindicated.
- c. Td: Tetanus toxoid with one third to one sixth the dose of diphtheria toxoid of other preparations; use in individuals ≥age 7 years in whom pertussis vaccine is contraindicated.

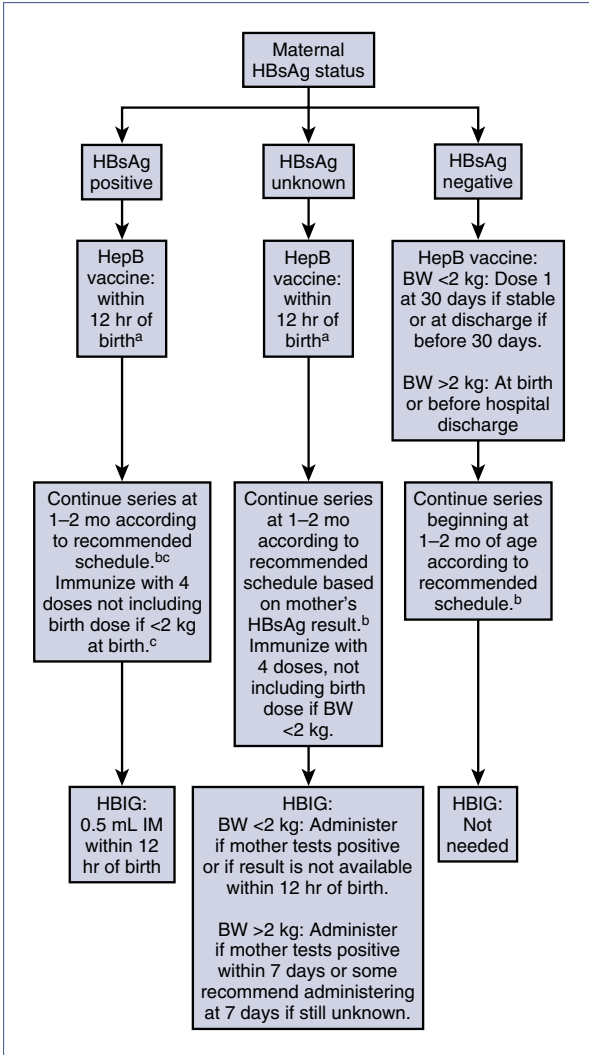
TABLE EC 16-B

**BLOOD PRODUCT ADMINISTRATION AND MMR/VARICELLA IMMUNIZATION**

Product/Indications	Route	Dose in mL/kg	Dose in mg/kg	Interval in Months
Tetanus TIG	IM	(250 U)	10	3
Hepatitis A Ig				
- Contact prophylaxis	IM	0.02	3.3	3
- International travel	IM	0.06	10	3
Hepatitis B HBIG	IM	0.06	10	3
Rabies RIG	IM	(20 IU/kg)	22	4
Varicella VariZIG	IM	(12.5 U/kg)	20–40	5
Measles Ig				
- Standard	IM	0.25	40	5
- Immunocompromised	IM	0.50	80	6
RSV (palivizumab)	IM		15	None
CMV Ig	IM	3	150	6
Blood transfusion				
- Washed RBCs	IV	10	Negligible	0
- RBCs, adenine-saline added	IV	10	10	3
- Packed RBCs	IV	10	20–60	5
- Whole blood	IV	10	80–100	6
- Plasma or platelets	IV	10	160	7
IVIG				
- Dosage for immune deficiencies or ITP	IV	—	300–400	8
- Dosage for ITP	IV	—	1000	10
- Dosage for ITP or Kawasaki	IV	—	1600–2000	11

CMV, Cytomegalovirus; HBIG, hepatitis B immune globulin; Ig, immunoglobulin; IM, intramuscular; ITP, idiopathic thrombocytopenic purpura; IV, intravenous; IVIG, intravenous immunoglobulin; RBCs, red blood cells; RIG, rabies immune globulin; RSV, respiratory syncytial virus; TIG, tetanus immune globulin; VariZIG, varicella-zoster immune globulin.

Modified from American Academy of Pediatrics. *Red Book: 2012 Report of the Committee on Infectious Diseases*. 29th ed. Elk Grove Village, Ill: AAP, 2012.



**FIGURE 16-4**

Management of neonates born to mothers with unknown or positive hepatitis B surface antigen (HbsAg) status. BW, Birth weight; HBIG, hepatitis B immune globulin; HepB, hepatitis B virus. <sup>a</sup>Only single antigen vaccine should be used. <sup>b</sup>A fourth vaccine dose is required if using combination vaccines. <sup>c</sup>Reimmunization may be required based on anti-HBs. Test at 9–18 mo of age. (Data from American Academy of Pediatrics. Red Book: 2012 Report of the Committee on Infectious Diseases. 29th ed. Elk Grove Village, Ill: AAP, 2012.)

- d. Tdap (Boostrix and Adacel): Tetanus and diphtheria toxoids combined with acellular pertussis vaccine. Boostrix can be given at age 10 years, Adacel at age 11 years.
2. **Contraindications:**
  - a. Encephalopathy within 7 days of administration of previous dose of DTaP.
  - b. Progressive neurologic disorder may merit permanent deferral of pertussis immunization. Reconsider pertussis immunization at each visit. Use DT or Td if pertussis vaccine is permanently deferred in children  $\geq$  age 1 year (children  $<1$  year should not receive DT; risk for diphtheria and tetanus is low in first year of life). After first birthday, initiate either DT or DTaP immunization, as clinically indicated.
- c. **Precautions:**
  - (1) Seizure disorder or seizures within 3 days of receiving a previous dose of DTaP:
    - (a) Poorly controlled or new-onset seizures: Defer pertussis immunization until seizure disorder is well controlled and progressive neurologic disorder is excluded; then give DTaP and antipyretics around the clock for 24 hours after immunization.
    - (b) Personal or family history of febrile seizures: Give DTaP and antipyretics around the clock for 24 hours after immunization.
  - (2) Temperature of  $40.5^{\circ}\text{C}$  ( $104.8^{\circ}\text{F}$ ) within 48 hours after immunization with a previous dose of DTaP
  - (3) Collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours of receiving a previous dose of DTaP
  - (4) Persistent inconsolable crying lasting 3 hours within 48 hours of receiving a previous dose of DTaP
  - (5) Guillain-Barré syndrome (GBS) within 6 weeks after a prior dose (however, completion of the primary series in children is usually justified)
- d. **Misconceptions (vaccines should be given):** Family history of seizures (see above) or family history of sudden infant death syndrome
3. **Side effects:** Substantially decreased with DTaP compared to DTP. Local tenderness (8%–11%), fever  $\geq 38.0^{\circ}\text{C}$  (8%–24%, more common in subsequent doses), anorexia (8%–11%), drowsiness (19%–33%), vomiting (4%–7%), crying  $\geq 1$  hour (1%–2%). Severe side effects of allergic reactions, persistent crying  $> 3$  hours, hypotonic-hyporesponsive episode, seizures, and body temperature  $> 40.5^{\circ}\text{C}$  that were more common with DTP vaccine are very rare with DTaP.<sup>5</sup>
4. **Administration:**
  - a. DTaP, DT, Td, or Tdap: Dose is 0.5 mL IM
  - b. Tetanus Ig (TIG): Dose is 10 mL/kg IM
5. **Special considerations:**
  - a. Tetanus prophylaxis in wound management (Table 16-3)
  - b. Pertussis exposure:
    - (1) Immunize all unimmunized or partially immunized close contacts  $<$  age 7 years and  $>$  age 10 years, according to the recommended



TABLE 16-3

INDICATIONS FOR TETANUS PROPHYLAXIS

Prior Tetanus Toxoid Doses	Clean, Minor Wounds		All Other Wounds	
	Tetanus Vaccine*	TIG	Tetanus Vaccine*	TIG
Unknown or < 3	Yes	No	Yes	Yes
≥3, last < 5 yr ago	No	No	No	No†
≥3, last 5–10 yr ago	No	No	Yes	No†
≥3, last > 10 yr ago	Yes	No	Yes	No†

\*Vaccine choice for child <age 7 yr is DTaP, and Tdap if >age 7 years (DT or Td if pertussis is contraindicated).

†Any child with HIV infection or who is within the first year after bone marrow transplantation should receive TIG for any tetanus-prone wound, regardless of vaccination status.

Modified from American Academy of Pediatrics. *Red Book: 2012 Report of the Committee on Infectious Diseases*. 29th ed. Elk Grove Village, Ill: AAP, 2012.

schedule. Give fourth dose of DTaP if third dose was given >6 months prior. Give booster dose of DTaP if last dose was given >3 years prior and child is <age 7 years.

- (2) Postexposure chemoprophylaxis with azithromycin, erythromycin or clarithromycin. Alternatives include trimethoprim-sulfamethoxazole (see Table 3.44 of the 2012 *Red Book* for more details<sup>2</sup>).

**B. *Haemophilus influenzae* Type B Immunoprophylaxis**

1. **Description:** The three licensed vaccines consist of a capsular polysaccharide antigen (PRP) conjugated to a carrier protein. It is not necessary to use the same formulation for the entire series.
  - a. PRP-OMP (PedvaxHIB): Conjugated to outer membrane protein of *Neisseria meningitidis*; requires only two doses in primary series (2 and 4 months) plus booster at 12–15 months. If PRP-OMP is used only for part of the immunization series, the recommended number of doses to complete the series is based on the other Hib vaccine used. Children without prior DTaP vaccine may respond better to PRP-OMP than to other formulations.
  - b. PRP-T (ActHIB): Conjugated to tetanus toxoid. Approved for ages 2–18 months.
  - c. PRP-T (Hiberix): Conjugated to tetanus toxoid. Approved as a booster dose in ages 15 months to 4 years.
2. **Contraindications:** None
3. **Side effects:** Local pain, redness, and swelling in 25% of recipients (mild, lasting <24 hours)
4. **Administration:** Dose is 0.5 mL IM
5. **Special considerations:**
  - a. See [Section IV.C](#).
  - b. Children with invasive Hib disease at age <24 months: Begin Hib immunization 1 month after acute illness and continue as if previously unimmunized. Vaccination is not required if invasive disease develops after age 24 months. Consider immunologic workup for any child with invasive Hib disease after completing the immunization series.

- c. Post exposure: Generally rifampin is recommended for unvaccinated household or daycare contacts <4 years of age.

### C. Hepatitis A Virus Immunoprophylaxis

1. **Description:** Two brands of HepA vaccine are available—Havrix and Vaqta (both preservative-free), which are licensed only for children  $\geq$  age 12 months.
2. **Contraindications:** Anaphylactic reaction to aluminum hydroxyphosphate sulfate, aluminum hydroxide, or neomycin.
3. **Side effects:** Local reactions are typically mild and include injection site tenderness (21%), redness, swelling and warmth (4%), rash (1%), fever (11%), and headache (<9%). No serious adverse events have been reported.<sup>6,7</sup>
4. **Administration:**
  - a. HepA vaccine: Dose is 0.5 mL IM for ages 1–18 years and 1 mL IM for  $\geq$  age 19 years
  - b. HepA Ig: Dose is 0.02 mL/kg (max dose, 5 mL) IM
5. **Special considerations:**
  - a. Preexposure immunoprophylaxis for travelers
    - (1) HepA vaccine is preferred for travelers  $\geq$ 12 months old; a single dose usually provides adequate immunity if time does not allow a second dose before travel.
    - (2) HepA Ig is protective for up to 5 months and can be given without vaccine to children <age 12 months before travel.
  - b. Postexposure immunoprophylaxis: If exposed in the last 2 weeks and <12 months old, should receive HepA Ig. If  $\geq$  age 12 months, should receive HepA vaccine. If it has been >2 weeks since exposure, no prophylaxis is indicated if <age 12 months, but HepA vaccine might be considered if  $\geq$  age 12 months and exposure could be ongoing.

### D. Hepatitis B Virus Immunoprophylaxis

1. **Description:**
  - a. HepB vaccine: Adsorbed HBsAg produced recombinantly. Different recombinant vaccines may be used interchangeably.
  - b. HBIG: Prepared from plasma containing high-titer anti-HBsAg antibodies and negative for antibodies to HIV and HCV.
2. **Contraindications:** Anaphylactic reaction to yeast
3. **Side effects:** Pain at injection site (3%–29%) or fever >37.7°C (1%–6%); immediate hypersensitivity reaction is very rare
4. **Administration:**
  - a. Recombivax: Dose is 5 mcg IM (0.5 mL pediatric formulation) for patients <age 20 years, 10 mcg IM (1 mL adult formulation)  $\geq$  age 20 years, and 40 mcg IM (1 mL dialysis formulation) for dialysis patients.
  - b. Engerix-B: Dose is 10 mcg IM (0.5 mL) for patients <age 20 years, 20 mcg IM (1 mL)  $\geq$  age 20 years, and 40 mcg IM (2 mL) for dialysis patients.
  - c. HBIG: Dose for infants is 0.5 mL IM; for older children, 0.06 mL/kg IM.

**5. Special considerations:**

- a. Infants of mothers who are HBsAg positive or unknown will have a different schedule (Fig. 16-4).
- b. See Table 16-4 for HepB prophylaxis after percutaneous exposure to blood.

**E. Human Papillomavirus Immunoprophylaxis**

**1. Description:** Two approved vaccines:

- a. HPV4 (Gardasil) vaccine protects against HPV types 6, 11, 16, and 18; administered to both females and males. Has efficacy against cervical, vulvar, and vaginal cancers caused by types 16 and 18; against genital warts, in females and males, caused by types 6 and 11.<sup>8</sup>
- b. HPV2 (Cervarix) has been approved for females and protects against HPV types 16 and 18.

**2. Contraindications:** Anaphylaxis to yeast.

- 3. Side effects:** Pain, swelling, and erythema at injection site (83%, 25%, and 25%, respectively), fever (10%), nausea (6%), dizziness (4%), syncope. Recommend observation for syncope for 15 minutes after administration.<sup>8</sup>

- 4. Administration:** Dose is 0.5 mL IM. First dose can be given at  $\geq$ age 9 years but recommended at age 11–12 years.

- 5. Special considerations:** Females or males with evidence of current HPV infection, such as cervical dysplasia or warts of a positive HPV DNA test, should still be immunized.

**F. Influenza Immunoprophylaxis**

Influenza strains can change year to year, particularly in time of pandemic flu; please refer to the CDC for up-to-date guidelines at [www.cdc.gov/flu/professionals/antivirals/index.htm](http://www.cdc.gov/flu/professionals/antivirals/index.htm).

**TABLE 16-4**

**HEPATITIS B VIRUS PROPHYLAXIS AFTER PERCUTANEOUS EXPOSURE TO BLOOD**

Exposed Person		HBsAg Status of Source of Blood	
		Negative	Unknown
Unimmunized	HBIG and HBV series	HBV series	HBV series
Previously immunized			
Known responder	No treatment	No treatment	No treatment
Known nonresponder	HBIG and HBV series	No treatment	Treat as if positive if known high risk source <i>OR</i> give HBIG $\times$ 2 (1 mo apart)*
Response unknown	Test exposed person for anti-HBsAg and HBV booster dose	No treatment	Test exposed person for anti-HBs: If inadequate, HBV booster dose If adequate ( $>10$ mIU/mL), no treatment

\*Preferred if already received two vaccine series with failure to respond.

Modified from American Academy of Pediatrics. *Red Book: 2012 Report of the Committee on Infectious Diseases*. 29th ed. Elk Grove Village, Ill: AAP, 2012.

1. **Description:** Activated and inactivated influenza vaccines are produced in embryonated eggs. Vaccines contain multiple viral strains (including both type A and type B strains) based on expected prevalent influenza strains for the upcoming winter:
  - a. Inactivated influenza vaccines: Split-virus vaccines with subvirion or purified surface antigen vaccines available; given IM to children  $\geq$  age 6 months
  - b. LAIV: Given intranasally to healthy children  $>$  age 2 years
2. **Contraindications:** Anaphylaxis to eggs is a contraindication to both IM and intranasal influenza vaccines; anaphylaxis to gelatin (which is in some influenza vaccines [look at package insert]). Contraindications specific to LAIV are pregnancy, asthma, children  $<$  age 5 years with wheezing in the past 12 months, immunocompromised, or on aspirin treatment:
  - a. **Precautions:** GBS within 6 weeks after a previous influenza vaccine dose
  - b. **Misconceptions (vaccines should be given):** Less severe or local manifestations of allergy to egg and pregnancy (give inactivated vaccine to pregnant patients)
3. **Side effects:** Fever 6–24 hours after immunization in children  $<$  age 2 years (10%–35%); rare in children  $>$  age 2 years. Local reactions are uncommon in children  $<$  13 years of age; 10% in children  $\geq$  13 years. There are no statistically significant differences observed between placebo and LAIV recipients for fever, rhinitis, or nasal congestion. If there is an association between the influenza vaccine and GBS, the risk is rare and  $\leq$  1–2 cases per million doses.
4. **Administration:** Give annually during the fall in preparation for winter influenza season:
  - a. Inactivated: Dose is 0.25 mL IM for ages 6–35 months and 0.5 mL IM for  $\geq$  age 3 years.
  - b. LAIV: Dose is 0.2 mL intranasally.
5. **Special considerations:**
  - a. **Chemoprophylaxis for influenza A and B:** High rates of resistance of influenza A and B to amantadine and rimantadine and of influenza A to oseltamivir cause recommendations to vary by season and location. Please refer to [www.cdc.gov/flu/professionals/antivirals/index.htm](http://www.cdc.gov/flu/professionals/antivirals/index.htm):
    - (1) Chemoprophylaxis against influenza A and B: Oseltamivir ( $\geq$  2 weeks) and zanamivir ( $\geq$  5 years)
    - (2) Chemoprophylaxis against influenza A only: Amantadine or rimantadine ( $\geq$  1 year)
    - (3) Indications for chemoprophylaxis:
      - (a) Unimmunized high-risk children, including those for whom the vaccine is contraindicated or children immunized  $<$  2 weeks before influenza outbreak.
      - (b) Unimmunized individuals in close contact with or providing care to high-risk individuals
      - (c) Immunodeficient individuals unlikely to have protective response to vaccine

- (d) Control of outbreaks in a closed setting
- (e) Immunized high-risk individuals if vaccine strain different from circulating strain
- (4) Chemoprophylaxis is not a substitute for immunization and does not interfere with the immune response to the inactivated virus vaccine. LAIV should not be administered until >48 hours after completing antiviral therapy for influenza.<sup>9</sup> Do not administer chemoprophylaxis until at least 2 weeks after administration of LAIV.
- b. Infants <age 6 months cannot be immunized. Close contacts should receive the vaccine.

### G. Japanese Encephalitis (JE) Immunoprophylaxis

See Expert Consult for more information.

### H. Measles/Mumps/Rubella Immunoprophylaxis

#### 1. Description:

- a. MMR: Combination vaccine composed of live attenuated viruses. Measles and mumps vaccines are grown in chick embryo cell culture; rubella vaccine is prepared in human diploid cell culture.
- b. Measles Ig: IM and IV immunoglobulin preparations contain similar concentration of measles antibody.
- c. Rubella Ig: Data showing decreased clinical infection, viral shedding, and rates of viremia are limited.<sup>2</sup>

#### 2. Contraindications: Anaphylactic reaction to neomycin or gelatin or immunocompromise

#### a. Precautions:

- (1) Recent (within 3–11 months, depending on product and dose) blood product administration (see Section IV.M).
- (2) Thrombocytopenia or history of thrombocytopenic purpura. In most instances, benefits of immunization will be much greater than potential risks, particularly because there is a higher risk of thrombocytopenia after measles or rubella disease.
- (3) Tuberculosis or positive purified protein derivative (PPD) tuberculin test. A theoretical basis exists for concern that measles vaccine might exacerbate tuberculosis. Before administering MMR to people with untreated active tuberculosis, initiating antituberculosis therapy is advisable.
- b. **Misconceptions (vaccines should be given):** PPD testing may be done on the day of immunization (otherwise, postpone PPD 4–6 weeks because of suppression of response), breast-feeding, pregnancy of mother of recipient, immunodeficiency in a family member or household contact, HIV infection, nonanaphylactic reactions to gelatin or neomycin, anaphylactic reaction to eggs (consider observing patient for 90 minutes after vaccine administration; skin testing is not predictive of hypersensitivity reaction and therefore is not recommended), history of seizures
- 3. **Side effects:** Fever to 39.4°C or higher develops in 5%–15% of immunized persons, usually between 6 and 12 days after immunization and

**1. Description:**

- a. A Vero cell culture–derived JE vaccine (JE-VC) for use in  $\geq$ age 17 years.
- b. Inactivated mouse brain–derived JE-MB that was licensed for use in children in the United States is no longer available. Other JE vaccines are manufactured and available for pediatric use in Asia but are not licensed in the United States.

**2. Contraindications:** Anaphylaxis to protamine sulfate.**3. Side effects:** Common are headache and myalgia, as well as local pain and tenderness.**4. Administration:** Dose is 0.25 mL IM for ages 2 months–2 years; dose is 0.5 mL IM for  $\geq$ age 3 years. Two doses are given 4 weeks apart. Boosters given yearly.**5. Special considerations:**

- a. Indications: Endemic areas include most rural areas of Asia. JE vaccine is recommended for travelers who plan to spend  $\geq$ 1 month in endemic areas during the JE season,  $<$ 1 month during times of an epidemic, or who will be outdoors frequently in rural areas.
- b. See <http://www.cdc.gov/japaneseencephalitis/vaccine/vaccineChildren.html> for more information on providing JE vaccines to U.S. children  $<$  age 17 years. Current options for children at high risk for JE include enrolling in JE-VC pediatric clinical trial, administering JE-VC off label, or referral to an international travelers' health clinic in Asia.

can last up to 5 days; febrile seizures are rare and occur 8–14 days after the first dose (fevers should be treated with antipyretics in those with a history of seizures); transient rash (5%); transient thrombocytopenia (1 in 25,000 to 1 in 2 million) 2–3 weeks after immunization; encephalitis and encephalopathy (<1 in 1 million).<sup>2</sup>

#### 4. **Administration:**

- a. MMR vaccine: Dose is 0.5 mL SQ.
- b. Measles Ig dose: Standard-dose Ig for children and pregnant women: 0.25 mL/kg (maximum dose, 15 mL) IM. High-dose Ig for immunocompromised children (including those with HIV infection): 0.5 mL/kg (maximum dose, 15 mL) IM. Not required if IVIG received within 3 weeks before exposure.

#### 5. **Special considerations:**

- a. Measles postexposure immunoprophylaxis:
  - (1) Vaccine prevents or modifies disease if given within 72 hours of exposure; it is the intervention of choice for measles outbreak.
  - (2) Measles Ig prevents or modifies disease if given within 6 days of exposure. It is indicated in susceptible household contacts, pregnant women, children <age 1 year, and immunocompromised individuals (including HIV-infected children), regardless of immunization status. It is not indicated for non immunocompromised contacts who have received one dose of the vaccine at  $\geq$ age 12 months.
- b. Rubella postexposure immunoprophylaxis:
  - (1) Rubella Ig can be considered in rubella-susceptible women exposed to confirmed rubella early in pregnancy if termination of the pregnancy is refused.

### I. **Meningococcal Immunoprophylaxis**

1. **Description:** Meningococcal vaccines are available against groups A, C, Y, and W-135 for children. No vaccine is available for group B because of poor immunogenicity:
  - a. Hib MenCY (Men Hibrix): Conjugate vaccine against Hib and meningococcus groups C and Y; for patients 6 weeks–18 months of age
  - b. MenACWY-D (Menactra): A tetravalent conjugate vaccine against groups A, C, Y, and W-135; for patients  $\geq$ 9 months of age
  - c. MenACWY-CRM (Menveo): A tetravalent conjugate vaccine against groups A, C, Y, and W-135; for patients  $\geq$ 2 years of age
  - d. MPSV4: A quadrivalent serogroup-specific vaccine against groups A, C, Y, and W-135; made from purified capsular polysaccharide antigen; for patients >5 years of age
2. **Contraindications:** Anaphalaxis to tetanus toxoid, diphtheria toxoid, or any natural rubber latex.
- a. **Precaution:** History of GBS
3. **Side effects:**
  - a. MenACWY: Mild localized erythema and pain lasting 1–2 days (occurs infrequently), fever (2%–5%), headache, irritability, fatigue

- b. Hib MenCY: Similar to Hib vaccine alone, with local injection-site pain, redness, and swelling common (15%–46%), as is irritability (62%–71%), drowsiness (49%–63%), loss of appetite (30%–34%), and fever (11%–26%)<sup>10</sup>
- 4. **Administration:** Dose is 0.5 mL IM for MenACWY and Hib MenCY, and 0.5 mL SQ for MPSV4.
- 5. **Special considerations:**
  - a. See [Sections IV.B](#) and [IV.F](#).
  - b. Postexposure immunoprophylaxis:
    - (1) Indications: Contact with the index case within 7 days before the onset of illness, including household, child care, and nursery school contacts; direct exposure to the index case's secretions, including mouth-to-mouth and unprotected endotracheal intubation, those who frequently slept in the home of the index case, and passengers next to the index case during airline flights longer than 8 hours.
    - (2) Treatment should be given within 24 hours of primary case diagnosis. Rifampin is the drug of choice with single dose ciprofloxacin or ceftriaxone as alternatives.
  - c. Hib MenCY or MCV4 can be given for outbreak control.

## J. Pneumococcal Immunoprophylaxis

### 1. Description:

- a. PCV13: Pneumococcal conjugate vaccine includes 13 purified capsular polysaccharides of *Streptococcus pneumoniae*, each coupled to a variant of diphtheria toxin. PCV7 had serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F, and serotypes 1, 3, 5, 6A, 7F, and 19A were added to PCV13.<sup>3</sup>
- b. 23PS: Purified capsular polysaccharide includes antigen from 23 serotypes (1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, and 33F<sup>3</sup>) of *S. pneumoniae*. Approved for children aged 2 years and older with certain underlying medical conditions.
- 2. **Contraindications:** None.
- 3. **Side effects:** Pain or erythema at injection site (>50%, with <10% interfering with limb movement); irritability (14%–86%), decreased appetite (16%–51%), decreased sleep (7%–47%), increased sleep (3%–72%), less commonly fever within 1–2 days after administration (1%–37%).<sup>11</sup>
- 4. **Administration:** Dose for both PCV13 and 23PS is 0.5 mL given IM. Concurrent administration of PCV13 and 23PS vaccines is not recommended.

### 5. Special considerations:

- a. See [Section IV.A](#).
- b. For children <age 60 months who received PCV7 for their primary series, they should complete the series with PCV13. If they have already received their full four-dose series of PCV7, they should receive one dose of PCV13 if <age 60 months (or older with a condition at special risk for pneumococcal disease).



## K. Poliomyelitis Immunoprophylaxis

### 1. Description:

- a. IPV: Inactivated injectable vaccine; contains three types of poliovirus grown in Vero cells and inactivated in formaldehyde.<sup>12</sup>
- b. OPV: Live viral oral vaccine; no longer available in the United States. Children who have received the appropriate number of doses of OPV in other countries should be considered adequately immunized.
2. **Administration:** Dose is 0.5 mL IM or SQ.
3. **Contraindications:** Anaphylactic reactions to neomycin, streptomycin, polymyxin B, 2-phenoxyethanol, and formaldehyde. OPV should generally not be given to immunocompromised children.
4. **Side effects:** 0%–29% local reactions, 0%–4% fever<sup>13</sup>; no serious side effects have been associated with use of IPV.

## L. Rabies Immunoprophylaxis

### 1. Description:

- a. Three rabies vaccines are available for prophylaxis: Human diploid cell vaccine (HDCV), rabies vaccine adsorbed (RVA), and purified chicken embryo cell vaccine (PCECV).
- b. Human rabies immune globulin (RIG): Antirabies Ig prepared from plasma of donors hyperimmunized with rabies vaccine.
2. **Contraindications:** Anaphylaxis to gelatin (present in some vaccines [look at package insert]). PCECV can be used if there is a serious allergic reaction to HDCV.
3. **Side effects:** Uncommon in children. In adults, local reactions in 15%–25%, mild systemic reactions (e.g., headache, abdominal pain, nausea, muscle aches, dizziness) in 10%–20%, and neurologic illness similar to GBS or focal central nervous system disorder (reported with HDCV but not believed to be causally related). Immune complex–like reaction (urticaria, arthralgia, angioedema, vomiting, fever, malaise) 2–21 days after immunization with HDCV is rare in primary series, but 6% after booster dose.
4. **Administration:**
  - a. Rabies vaccines: Dose is 1 mL IM. Do not administer in same part of body or in same syringe as RIG.
  - b. RIG: Dose is 20 IU/kg. Infiltrate around the wound and give remainder IM.
5. **Special considerations:**
  - a. Preexposure prophylaxis: Indicated for high-risk groups, including veterinarians, animal handlers, laboratory workers, children living in high-risk environments, those traveling to high-risk areas, and spelunkers:
    - (1) Three injections of HDCV or PCEC vaccine on days 0, 7, and 21 or 28.
    - (2) Rabies serum antibody titers should be followed at 6-month intervals for those at continuous risk and at 2-year intervals for those with risk for frequent exposure; give booster doses only if titers are nonprotective.

TABLE 16-5

## RABIES POSTEXPOSURE PROPHYLAXIS

Animal Type	Evaluation and Disposition of Animal	Postexposure Prophylaxis Recommendations
Dogs, cats, ferrets	Healthy and available for 10 days' observation. Rabid or suspected rabid; euthanize animal and test brain. Unknown (escaped).	Do not begin prophylaxis unless animal develops signs of rabies. Provide immediate immunization and RIG. Consult public health officials.
Skunk, raccoon, bat,* fox, woodchuck, most other carnivores	Regard as rabid unless geographic area is known to be free of rabies or until animal is euthanized and proven negative by testing.	Provide immediate immunization and RIG.†
Livestock, rodents, rabbit, other mammals	Consider individually.	Consult public health officials; these bites rarely require treatment.

\*In the case of direct contact between a human and a bat, consider prophylaxis even if a bite, scratch, or mucous membrane exposure is not apparent.

†Treatment may be discontinued if animal fluorescent antibody is negative.

Modified from American Academy of Pediatrics. *Red Book: 2012 Report of the Committee on Infectious Diseases*. 29th ed. Elk Grove Village, Ill: AAP, 2012.

b. Postexposure prophylaxis (Table 16-5):

- (1) General wound management: Clean immediately with soap and water and flush thoroughly. Avoid suturing wound unless indicated for functional reasons. Consider tetanus prophylaxis and antibiotics if indicated. Report all patients suspected of rabies infection to public health authorities.
- (2) Indications: Infectious exposures include bites, scratches, or contamination of open wound or mucous membrane with infectious material of a rabid animal or human.
- (3) Vaccine for postexposure prophylaxis:
  - (a) Unimmunized: 1 mL IM on days 0, 3, 7, and 14. The fifth dose is only necessary for children who are immunosuppressed and should be given on day 28.
  - (b) Previously immunized (including preexposure and postexposure): 1 mL IM on days 0 and 3. Do not give RIG.
- (4) Vaccine and RIG should be given jointly except in previously immunized patients (no RIG required). If vaccine is not immediately available, give RIG alone and vaccinate later. If RIG is unavailable, give vaccine alone. RIG may be given within 7 days after initiating immunization.

### M. Respiratory Syncytial Virus (RSV) Immunoprophylaxis

1. **Description:** Palivizumab (monoclonal RSV-Ig) is a humanized mouse monoclonal IgG to RSV.
2. **Contraindications:** None.
3. **Side effects:** Comparable to placebo; upper respiratory tract infection, otitis media, fever, rhinitis, and liver function test elevation occurred 1%–3% more commonly than with placebo.

4. **Administration:** Dose is 15 mg/kg IM. Give palivizumab at onset of RSV season (November 1 for most of the United States, July 1 for southeast Florida, September 15 for north central and southwest Florida) and then monthly as indicated.
5. **Special considerations:**
  - a. Indications<sup>13</sup>:
    - (1) Infants and children <age 2 years with chronic lung disease (CLD) who have required medical therapy (oxygen, bronchodilators, diuretics, or corticosteroids) within the 6 months before the RSV season. These children should receive a maximum of five doses. Data are limited, but these patients may also benefit from prophylaxis during a second RSV season.
    - (2) Infants <32 weeks' estimated gestational age (EGA) at birth who do not have CLD may benefit from prophylaxis with palivizumab. These children should receive a maximum of five doses:
      - (a) EGA < 29 weeks: If <12 months at the start of RSV season
      - (b) EGA 29 to <32 weeks: If <6 months at the start of RSV season
    - (3) Infants 32 weeks to <35 weeks EGA who are <age 3 months at the start of the RSV season and who are likely to have increased RSV exposure (child care attendance or siblings < 5 years of age). These children should receive a maximum of three doses, none being after 3 months of age.
    - (4) Infants with congenital abnormalities of the airway or neuromuscular disease and should receive a maximum of five doses during the first year of life.
    - (5) Infants with hemodynamically significant cyanotic or acyanotic congenital heart disease who are ≤24 months of age should be considered for prophylaxis. This includes children who:
      - (a) Are receiving medication for treatment of congestive heart failure.
      - (b) Have moderate to severe pulmonary hypertension.
      - (c) Have a cyanotic heart lesion. Children who have undergone a surgical procedure where bypass was used should receive a postoperative dose of palivizumab as soon as clinically stable.
    - (6) There are no specific recommendations for severely immunocompromised children, but they may benefit from prophylaxis.

## N. Rotavirus Immunoprophylaxis

1. **Description:** Two vaccines available
  - a. RotaTeq (RV5): Pentavalent live viral vaccine containing five reassortant human and bovine rotavirus strains in the form of an oral solution given in three doses
  - b. Rotarix (RV1): Live human attenuated rotavirus in the form of an oral solution given in two doses
2. **Contraindications:** Severe allergic reaction to latex (RV1 only)
  - a. **Precautions:** Preexisting chronic gastrointestinal disease, history of intussusception, spina bifida, or bladder exstrophy

- b. **Misconceptions (vaccines should be given):** Breast-feeding or immunodeficient family member/contact
- 3. **Side effects:** Diarrhea (24%), vomiting (15%), otitis media (14.5%), nasopharyngitis (7%), and bronchospasm (1%). Adverse events among Rotarix and placebo occurred at similar rates.<sup>15,16</sup>
- 4. **Administration:**
  - a. RotaTaq: Dose is 2 mL orally (PO). Vaccine is packaged in single-dose tubes to be administered without dilution. Do not readminister if infant spits out or vomits dose. Given in three doses, typically at 2, 4, and 6 months of age.
  - b. Rotarix: Dose is 1 mL PO. Vaccine is packaged to be reconstituted only with the accompanying diluent. If the infant spits out or vomits a dose, a single replacement dose at the same visit may be considered. Given in two doses, typically at 2 and 4 months of age.
- 5. **Special considerations:**
  - a. Premature infants can begin the series at 6 weeks of chronologic age if clinically stable.
  - b. Infants who received antibody-containing products can receive the first dose 42 days after the product was given.

#### O. Tuberculosis Immunoprophylaxis

See Expert Consult for more information.

#### P. Typhoid Fever Immunoprophylaxis

- 1. **Description:** Two typhoid vaccines are available and induce a protective response in 50%–80% of recipients:
  - a. Vi capsular polysaccharide vaccine (ViCPS) administered IM for children  $\geq$  age 2 years
  - b. Oral live attenuated vaccine (Ty21a) for  $\geq$  age 6 years
- 2. **Contraindications:** Immunocompromised (for Ty21a only)
  - a. **Other precautions:** Taking antibiotics that would be active against *Salmonella typhi* (for Ty21a only)
- 3. **Side effects:** For children receiving ViCPS, local soreness/pain (13%–14%), erythema (7%), induration (3%), impaired limb use not found, subjective fever (3%), and decreased activity (2%)<sup>17</sup>
- 4. **Administration:**
  - a. ViCPS: Dose is 0.5 mL IM for children  $\geq$  age 2 weeks before potential exposure. Booster dose every 2 years.
  - b. Ty21a: Four capsules that must be swallowed whole (one taken every other day) and finished  $\geq$  1 week before potential exposure. Booster series every 5 years.
- 5. **Special considerations:** Indicated for travelers to endemic areas

#### Q. Varicella Immunoprophylaxis

- 1. **Description:**
  - a. Vaccine: Cell-free live attenuated varicella virus vaccine
  - b. Varicella-zoster immune globulin (VarizIG): Prepared from plasma containing high-titer antiviral antibodies

1. **Description:** Attenuated live culture preparation of the bacille Calmette-Guérin (BCG) strain of *Mycobacterium bovis*. Given after birth in areas where tuberculosis is common. Not used routinely in the United States.
2. **Contraindications:** Immunocompromised (although some countries have HIV as a precaution, given higher risk of severe disease from tuberculosis and recommend BCG vaccine).
3. **Side effects:** Common are axillary or cervical lymphadenopathy and pustule formation at injection site. Rarely can cause disseminated BCG infection or BCG osteitis (0.01–43 cases per million doses, but more common in immunocompromised patients).
4. **Administration:** Mix 2 mL of sterile water with 1 vial of vaccine (50 mg) for patients aged <1 year, and 1 mL of sterile water with 1 vial of vaccine (50 mg) for those ≥age 1 year, given percutaneously with a multiple puncture device in the deltoid region.
5. **Special considerations:** See Chapter 17 for more information about tuberculosis testing and treatment.

2. **Contraindications:** Anaphylactic reaction to neomycin or gelatin, or immunocompromised:
  - a. **Other precautions:** Recent (within 3–11 months, depending on product and dose) blood product administration (see Section IV.M)
  - b. **Misconceptions (vaccines should be given):** Pregnancy of mother of recipient, immunodeficiency in a household contact (including HIV infection)
3. **Side effects:** Injection site reactions (20%), fever (15%), mild varicelliform rash within 5–26 days of vaccine administration (3%–5%), although most thought to be due to wild-type VZV infection. Vaccine rash often very mild, but patient may be infectious; reversion to wild-type virus has not been reported.<sup>18</sup>
4. **Administration:**
  - a. Varicella vaccine: Dose is 0.5 mL SQ.
  - b. VariZIG: Dose is 12.5 units/kg IM (maximum dose, 625 U; minimum dose, 125 U). If VariZIG is unavailable, can give IVIG 400 mg/kg IV.
5. **Special considerations:**
  - a. Do not give vaccine for 5 months after VariZIG; do not give concurrently with VariZIG. Avoid salicylates for 6 weeks after vaccine administration if possible. Avoid antiviral treatment for 21 days after vaccination.
  - b. Consider vaccine in household contacts of immunocompromised hosts. If a rash develops in the immunized person, avoid direct contact if possible.
  - c. Postexposure prophylaxis:
    - (1) Candidates for VariZIG or acyclovir who have had significant exposure include immunocompromised individuals without a history of varicella or varicella immunization, susceptible pregnant women, newborn infants, hospitalized preterm infants
      - (a) Significant exposures: Household contact, face-to-face indoor play, onset of varicella in the mother of a newborn from 5 days before to 2 days after delivery (even if mother received VariZIG during pregnancy), hospital exposures (roommate, face-to-face contact with infectious individual, visit by contagious individual, or intimate contact with person with active zoster lesions)
    - (2) Potential interventions for people without evidence of immunity include:
      - (a) Varicella vaccine ideally administered within 3 days but up to 5 days after exposure for immunocompetent children.
      - (b) VariZIG given as one dose up to 96 hours after exposure (give as soon as possible). IVIG can be used if VariZIG is unavailable.
      - (c) Oral acyclovir can also be given beginning 7 days after exposure.

## R. Yellow Fever Immunoprophylaxis

1. **Description:** Live attenuated virus vaccine approved for children  $\geq$  age 6 months but recommended for children  $\geq$  age 9 months
2. **Contraindications:** Anaphylaxis to eggs or gelatin. Skin testing with yellow fever vaccine is recommended before administration in children with a

history of immediate hypersensitivity reaction (e.g., anaphylaxis or generalized urticaria) to eggs. Immunocompromised individuals also at risk:

- a. **Precautions:** Age 6–8 months (see below), pregnancy, breast-feeding, or asymptomatic HIV infection
3. **Side effects:** Yellow fever vaccine rarely found to be associated with risk of viscerotropic disease (multiple-organ system failure) and neurotropic disease (postvaccine encephalitis). Increased risk of adverse events in persons of any age with thymic dysfunction and an increased risk of postvaccine encephalitis in younger children (<9 months).
4. **Administration:** Dose is 0.5 mL IM. Booster necessary every 10 years.
5. **Special considerations:**
  - a. Yellow fever is endemic in areas of sub-Saharan Africa and South America. Vaccine is required by some countries as a condition of entry.
  - b. Vaccine is available in the United States only in designated centers. A list of centers that provide yellow fever vaccine (and usually other travel vaccines) can be found at <http://wwwnc.cdc.gov/travel/yellow-fever-vaccination-clinics/search.htm>.

### S. Combination Vaccines

1. **Comvax = PRP-OMP (Hib)/HepB:** 6 weeks–71 months of age
2. **Kinrix = DTaP-IPV:** Given commonly as fifth dose of DTaP and fourth dose of IPV at age 4–6 years
3. **Pediarix = DTaP/HepB/IPV:** 6 weeks–7 years of age; minimum interval is 6 weeks
  - a. Higher rates of fever are reported with combination vaccine than the vaccines administered separately.
4. **Pentacel = DTaP-IPV/PRP-T (Hib):** 6 weeks–4 years of age
5. **Proquad = measles/mumps/rubella/varicella<sup>17</sup>:** 12 months–12 years of age:
  - a. Unless caregiver prefers MMRV vaccine, CDC recommends that MMR and varicella vaccines be administered separately for the first dose in 12- to 47-month child, owing to studies showing increased risk for febrile seizure with combination vaccine in this age group. Combination MMRV vaccine can be used for second dose or as first dose for children >age 48 months.
6. **TriHIBit = DTaP/PRP-T (Hib):** Fourth dose of Hib and DTaP series between 15–18 months
7. **Twinnix = HepA/HepB:** ≥18 years of age. Administered in a three-dose schedule given at 0, 1 month, and 6 months; dose is 1 mL
8. **MenHibirix = Hib / MenCY:** 6 weeks to 23 months of age

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18. Merck package insert for Varivax.
19. Merck package insert for ProQuad (measles, mumps, rubella, and varicella live virus vaccine).



# Chapter 17

## Microbiology and Infectious Disease

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 See additional content on Expert Consult

### I. MICROBIOLOGY

#### A. Collection of Specimens for Blood Culture

1. **Preparation:** To minimize contamination, clean venipuncture site with 70% isopropyl ethyl alcohol. Apply tincture of iodine or 10% povidone-iodine and allow to dry for at least 1 minute, or scrub site with 2% chlorhexidine for 30 seconds and allow to dry for 30 seconds. Clean blood culture bottle injection site with alcohol only.
2. **Collection:** Two sets of cultures of equal blood volume should be obtained for each febrile episode, based on patient weight: <8 kg, 1–3 mL each; 8–13 kg, 4–5 mL; 14–25 kg, 10–15 mL each; >25 kg, 20–30 mL each (modified from Kaditis et al. 1996<sup>1</sup>). Total blood volume drawn should not exceed more than 1% of patient's total blood volume.

#### B. Rapid Microbiologic Identification of Common Aerobic Bacteria (Fig. 17-1)

#### C. Choosing Appropriate Antibiotic Based on Sensitivities

1. **Minimum inhibitory concentration (MIC):** Lowest concentration of an antimicrobial agent that prevents visible growth; MICs are unique to each agent. Antibiotic selection should be based on whether agent is "susceptible" rather than MIC.
2. **See Tables 17-1 through 17-6 for spectrum of activity of commonly used antibiotics.**<sup>2,3</sup>

**Note:** Antibiotic sensitivities can vary greatly with local resistance patterns. Follow published institutional guidelines and culture results for individual patients and infections. When possible, always use agent with narrowest spectrum of activity particularly when organism susceptibilities are known.

### II. INFECTIOUS DISEASE

#### A. Fever Without Localizing Source: Evaluation and Management Guidelines

1. **Age < 28 days:** Hospitalize for full evaluation (Fig. 17-2). Owing to the greater risk of serious bacterial infections in young infants with fever, a conservative approach is warranted.
2. **Age 29–90 days:** Well-appearing infants who meet low-risk criteria may potentially be managed as outpatients if reliable follow-up and monitoring is ensured.

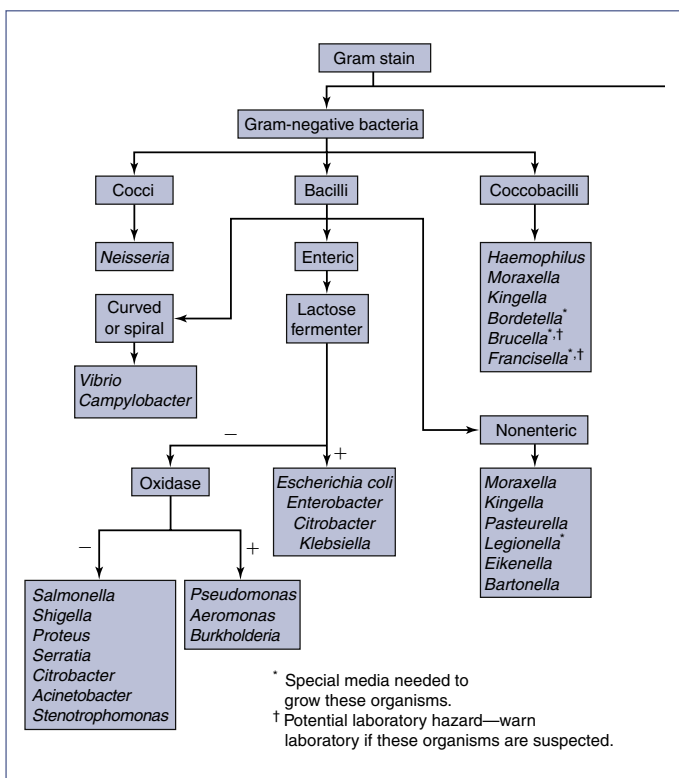
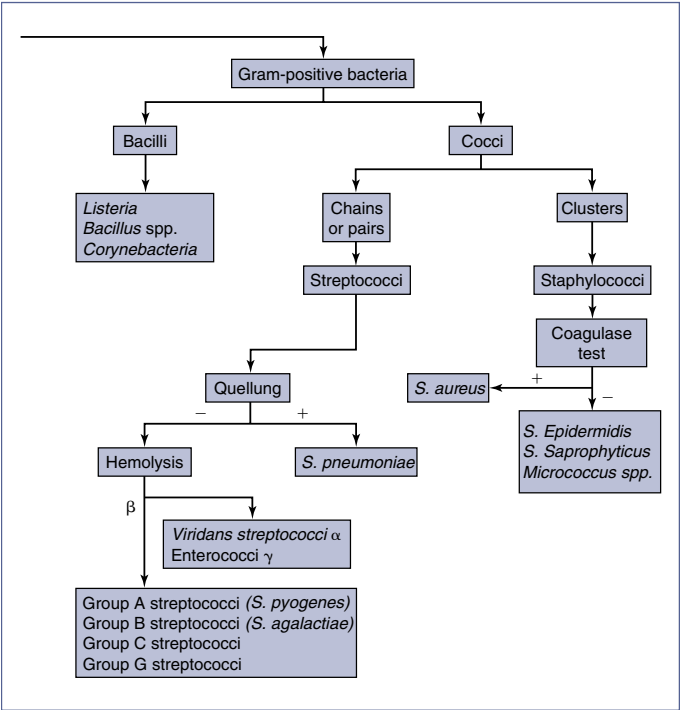


FIGURE 17-1

Algorithm demonstrating identification of aerobic bacteria.

3. **Age > 90 days:** Traditionally, similar risk-stratification strategies were advocated and used to aid evaluation and management of febrile children >90 days of age. However, the marked decline in invasive infections due to *Haemophilus influenzae* type b and *Streptococcus pneumoniae*, since introduction of conjugate vaccines, has significantly reduced the likelihood of serious bacterial infection in a well-appearing child within this age group:

- If ill-appearing without source of infection identified, consider admission and empirical antimicrobial therapy.
- If source of infection identified, treat accordingly.
- If well-appearing and without foci of infection, many experts now advocate urinalysis + urine culture as the only routine diagnostic test if reliable



**FIGURE 17-1, cont'd**

follow-up and monitoring is ensured, including all females and uncircumcised males <age 2 years, all circumcised males <age 6 months, and all children with known genitourinary tract abnormalities.<sup>4,5</sup>

**B. Intrauterine and Perinatal Infections**

- 1. Intrauterine (congenital) infections:** The acronym TORCH (toxoplasmosis, other, rubella, cytomegalovirus [CMV], herpes simplex virus [HSV]) is used to describe a group of infections (including a large number that fall under "other") outlined individually in [Table 17-7](#). These infections often present in the neonate with overlapping findings: intrauterine growth retardation (IUGR), hematologic insult, ocular abnormalities, central nervous system (CNS) signs, and other organ system involvement (e.g., pneumonitis, myocarditis, nephritis, hepatitis).<sup>6-8</sup> Workup and management of these infections is detailed in [Table 17-7](#).

TABLE 17-1

**β-LACTAMS**

	Gram-Positive Organisms	Gram-Negative Organisms	Anaerobes	Spirochetes
<b>PENICILLINS</b>				
Natural penicillins (Pen G or Pen V)	<i>Streptococcus pyogenes</i> , <i>Streptococcus agalactiae</i> , <i>Streptococcus pneumoniae</i> (with about 10%–20% resistance), <i>Listeria</i>	<i>Neisseria meningitidis</i>	Oral but not all gut anaerobes (gut organisms can make β-lactamases)	Syphilis Leptospirosis
Nafcillin, oxacillin, dicloxacillin	MSSA, CoNS (high levels of resistance)			
Amoxicillin, ampicillin	<i>S. pyogenes</i> , <i>S. agalactiae</i> , <i>S. pneumoniae</i> , <i>Viridans streptococcus</i> , <i>Listeria</i> , <i>Enterococcus fecalis</i>	Non-β-lactamase-producing <i>Escherichia coli</i> , <i>Haemophilus influenzae</i> , <i>Proteus</i>	Oral but not all gut anaerobes (gut organisms can make β-lactamases)	<i>Borrelia burgdorferi</i> (Lyme disease)
Amoxicillin/clavulanic acid (Augmentin), ampicillin/ sulbactam (Unasyn)	Amoxicillin coverage plus MSSA	β-Lactamase-producing Gram-negative organisms (>95% of <i>E. coli</i> , <i>H. influenzae</i> )	Oral and gut anaerobes	
Piperacillin/tazobactam (Zosyn), ticarcillin/clavulanate (Timentin)	<i>E. fecalis</i> , MSSA, <i>S. pyogenes</i> , <i>S. agalactiae</i>	β-Lactamase-producing Gram-negative organisms (majority of <i>E. coli</i> , <i>H. influenzae</i> ) as well as <i>Pseudomonas</i> , <i>Serratia</i> , <i>Citrobacter</i> (varies based on local epidemiology)	Oral and gut anaerobes	
<b>CEPHALOSPORINS</b>				
Do not cover LAME ( <i>Listeria</i> , Atypicals such as <i>Mycoplasma</i> and <i>Chlamydia</i> , MRSA [except for ceftaroline], and Enterococci)				
First-generation: cephalexin, cefazolin	MSSA, <i>S. pyogenes</i> , <i>S. agalactiae</i>	Very good coverage of enteric Gram-negative organisms (e.g., <i>E. coli</i> , <i>Klebsiella</i> , etc.), <i>Moraxella catarrhalis</i>		

Continued

TABLE 17-1

**β-LACTAMS (Continued)**

	Gram-Positive Organisms	Gram-Negative Organisms	Anaerobes	Spirochetes
Second-generation: cefuroxime ("true"), cefotetan and cefoxitin ("derived")	True, same as first-generation Derived, little activity	β-Lactamase-producing Gram-negative organisms ( <i>E. coli</i> , <i>H. influenzae</i> , <i>Klebsiella</i> spp., <i>Proteus</i> spp., <i>M. catarrhalis</i> , etc.), <i>Enterobacter</i> , some <i>Neisseria</i> spp.	Derived have moderate activity (poor coverage of gut anaerobes)	
Third-generation: ceftriaxone, cefotaxime, ceftazidime IV (oral: Suprax = cefixime, Vantin = cefpodoxime, Omnicef = cefdinir) <i>Good CNS penetration</i>	<i>S. pneumoniae</i> (majority), <i>S. pyogenes</i> , <i>S. agalactiae</i> , <i>Viridans streptococcus</i> , other streptococci	Ceftriaxone/cefotaxime and orals: β-lactamase-producing Gram-negatives ( <i>E. coli</i> , <i>H. influenzae</i> , <i>M. catarrhalis</i> , <i>Klebsiella</i> , <i>Proteus</i> , <i>Neisseria</i> , etc.) Ceftazidime: β-lactamase-producing Gram-negatives, <i>Pseudomonas</i>	None	<i>B. burgdorferi</i>
Fourth-generation: cefepime <i>Good CNS penetration</i>	Same as third-generation plus MSSA	β-Lactamase-producing Gram-negatives, <i>Pseudomonas</i>		
<b>CARBAPENEMS</b>				
Meropenem, imipenem	MSSA, <i>S. pneumoniae</i> , <i>S. pyogenes</i> , <i>S. agalactiae</i> , <i>Enterococcus</i>	β-Lactamase-producing Gram-negatives, including some very resistant <i>Pseudomonas</i> spp., <i>Acinetobacter</i> spp., <i>Serratia</i> spp., <i>Klebsiella</i> spp., <i>E. coli</i>	Oral and gut (not <i>Clostridium difficile</i> )	
Ertapenem	MSSA	β-Lactamase-producing Gram-negatives (less active against <i>Pseudomonas</i> and <i>Acinetobacter</i> than other carbapenems)	All oral and gut (not <i>C. difficile</i> )	
<b>MONOBACTAMS</b>				
Aztreonam		Covers most aerobic Gram-negative bacilli, including about 2/3 of <i>Pseudomonas</i> spp.		

CNS, Central nervous system; CoNS, coagulase-negative staphylococci; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*.

TABLE 17-2

## FLUOROQUINOLONES

	Gram-Positive Organisms	Gram-Negative Organisms	Anaerobes	Other
Ciprofloxacin	<i>Bacillus</i> spp., including <i>Bacillus anthracis</i>	Broad coverage, including <i>Pseudomonas</i> ; emerging <i>Neisseria</i> resistance		<i>Mycobacterium</i> , <i>Bartonella</i> , <i>Rickettsia</i>
Levofloxacin	Excellent <i>Streptococcus pneumoniae</i> coverage; some MSSA and <i>S. epidermidis</i> coverage	Almost same coverage as ciprofloxacin		Great atypical coverage
Moxifloxacin	Same as levofloxacin	Good enteric coverage; poor <i>Pseudomonas</i> coverage	Best anaerobic coverage of quinolones	Good for MTB and MAI

MAI, *Mycobacterium avium* subsp. *intracellulare*; MSSA, methicillin-sensitive *Staphylococcus aureus*; MTB, *Mycobacterium tuberculosis*.

TABLE 17-3

## MACROLIDES

	Gram positive organisms	Atypicals	Others
Clarithromycin	Reasonably good against <i>Streptococcus pneumoniae</i> (-50-70%)	<i>Mycoplasma</i> , <i>Chlamydia pneumoniae</i> , <i>Legionella</i>	<i>Bartonella henslae</i> , <i>Bordetella pertussis</i> , <i>Campylobacter</i> , and <i>H. flu</i>
Erythromycin	Same as clarithromycin	Above and <i>Chlamydia trachomatis</i>	Diphtheria, Entamoeba histolytica
Azithromycin	Same as clarithromycin	Above plus <i>Toxoplasmosis</i> (with pyrimethamine)	<i>N. gonorrhea</i> , <i>Treponema pallidum</i> (Syphilis), <i>Haemophilus ducreyi</i> (chancres)

TABLE 17-4

## TETRACYCLINES

	Gram-Positive Organisms	Atypicals	Others
Doxycycline and tetracycline	Some streptococci, pneumococci, MSSA, MRSA, <i>Propionibacterium acnes</i>	<i>Mycoplasma</i> , <i>Chlamydia</i> , <i>Legionella</i>	<i>Haemophilus influenzae</i> , some anaerobic activity, <i>Borrelia burgdorferi</i> , <i>Rickettsia</i> , <i>Francisella tularensis</i> (tularemia), <i>Vibrio</i> , <i>Helicobacter pylori</i>

MRSA, Methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*.

TABLE 17-5

## AMINOGLYCOSIDES

	Gram-Negative Organisms
Gentamicin and streptomycin	Almost all Gram-negative organisms; synergy with ampicillin for <i>Enterococcus</i>
Tobramycin and amikacin	Almost all Gram-negative organisms

**TABLE 17-6**  
**SINGLE DRUG CLASS**

	<b>Gram-Positive Organisms</b>	<b>Gram-Negative Organisms</b>	<b>Other</b>
Clindamycin	Broad Gram-positive coverage: MRSA, MSSA, <i>Streptococcus pyogenes</i> , <i>Streptococcus agalactiae</i>	Second-line agent for <i>Campylobacter jejuni</i> and <i>Gardnerella vaginalis</i>	Oral anaerobes; some <i>Chlamydia trachomatis</i> and <i>Mycoplasma</i> spp. coverage; and <i>Gardnerella vaginalis</i>
Metronidazole	Anaerobic Gram-positive organisms: <i>Clostridium</i> spp., <i>Peptostreptococcus</i>	<i>Helicobacter pylori</i> and gram-negative anaerobes: <i>Bacteroides</i> spp., <i>Prevotella</i> , <i>Fusobacterium</i>	<i>Entamoeba histolytica</i> , <i>Giardia lamblia</i> , <i>Trichomonas vaginalis</i> , and <i>G. vaginalis</i>
Linezolid	MRSA, MSSA, <i>Enterococcus</i> (including VRE), CoNS, <i>S. pyogenes</i> , <i>S. agalactiae</i> , <i>Streptococcus pneumoniae</i> , <i>S. viridans</i>	None	<i>Mycobacterium</i> spp., <i>Nocardia</i>
Vancomycin	MRSA, MSSA, <i>Enterococcus</i> (except VRE), CoNS, <i>S. pyogenes</i> and <i>agalactiae</i> , <i>S. pneumoniae</i> , <i>C. difficile</i> (orally)	None	
Trimethoprim + Sulfamethoxazole	MRSA, MSSA, <i>Listeria</i> (second choice if PCN allergy)	Many Gram-negative bacilli, including <i>Stenotrophomonas</i>	PCP ( <i>Pneumocystis jirovecii</i> ), <i>Toxoplasma gondii</i> , <i>Nocardia</i>

CoNS, Coagulase-negative staphylococci; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*; PCN, penicillin; PCP, *Pneumocystis pneumonia*; VRE, vancomycin-resistant *Enterococcus*.

2. **Perinatal viral infections:** Perinatal varicella-zoster virus (VZV), HSV, enterovirus, and CMV infections can be severe, with profound morbidity and mortality. Although VZV, HSV, hepatitis B, and hepatitis C can all cause intrauterine (congenital) infection, perinatal infection around the time of birth is more common. It can be difficult to clinically distinguish neonatal VZV and HSV lesions.<sup>9</sup> Workup and management of these infections is detailed in [Table 17-8](#).
3. **Group B streptococcal (GBS) infection:**
- a. Adequate maternal intrapartum prophylaxis is intravenous (IV) penicillin, ampicillin, or cefazolin  $\geq 4$  hours before delivery.<sup>9</sup> [Fig. 17-3](#) shows an algorithm for secondary prevention of early-onset GBS disease in newborns.
  - b. Late-onset GBS: See [Table 17-9](#).

TABLE EC 17-A

## GUIDE FOR INTERPRETATION OF THE SYPHILIS SEROLOGY OF MOTHERS AND THEIR INFANTS

Nontreponemal Test (e.g., VDRL, RPR)		Treponemal Test (e.g., FTA-ABS, TP-PA)		Interpretation*
Mother	Infant	Mother	Infant	
—	—	—	—	No syphilis or incubating syphilis in mother or infant
+	+	—	—	No syphilis in mother or infant (false-positive nontreponemal test with passive transfer to infant)
+	+ or —	+	+	Maternal syphilis with possible infant infection, mother treated for syphilis during pregnancy, or mother with latent syphilis and possible infection of infant†
+	+	+	+	Recent or previous syphilis in the mother; possible infant infection
—	—	+	+	Mother successfully treated for syphilis before or early in pregnancy, or mother with false-positive serologic test result; infant syphilis unlikely

\*Table presents a guide and not the definitive interpretation of serologic tests for syphilis in mothers and their newborns.

Other factors that should be considered include timing of maternal infection, nature and timing of maternal treatment, quantitative maternal and infant titers, and serial determination of nontreponemal test titers in both mother and infant, and sexual history of mother.

†Mothers with latent syphilis may have nonreactive nontreponemal tests.

FTA-ABS, Fluorescent treponemal antibody absorption; RPR, rapid plasma reagin; TP-PA, *Treponema pallidum* particle agglutination; VDRL, Venereal Disease Research Laboratory test.

From American Academy of Pediatrics. Pickering LK, Baker CJ, Kimberlin DW, et al, eds. *Red Book: 2009 Report of the Committee on Infectious Diseases*. 28th ed. Elk Grove Village, Ill: AAP, 2009.



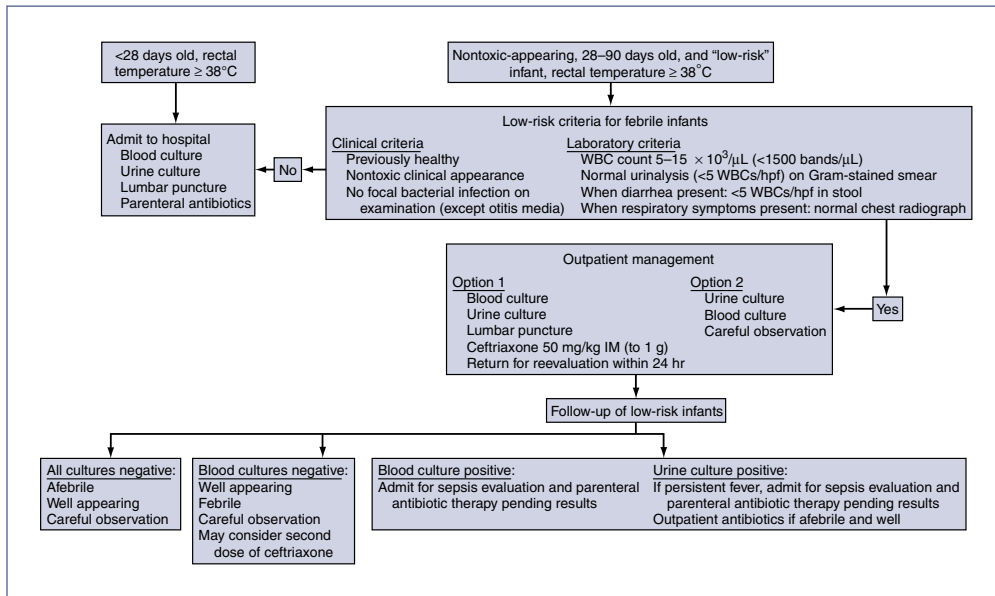


FIGURE 17-2

Algorithm for management of a previously healthy infant ≤90 days of age with a fever without localizing signs. This algorithm is a suggested but not exhaustive approach. hpf, High-power field. (Modified from Baraff LJ. Management of fever without source in infants and children. *Ann Emerg Med.* 2000;36:602-614; and Baraff LJ. Management of infants and young children with fever without source. *Pediatr Ann.* 2008;37:673-679.)

TABLE 17-7

CONGENITAL INFECTIONS

Infective Agent	Clinical Findings	Diagnostic Testing	Therapy
Toxoplasmosis	70%–90% asymptomatic at birth; maculopapular rash, generalized lymphadenopathy, hepatosplenomegaly, jaundice, pneumonitis, petechiae, and thrombocytopenia. Can develop hydrocephalus, microcephaly, chorioretinitis, seizures, and hearing loss	<ul style="list-style-type: none"> <li>• Presence of immunoglobulin (Ig) M or IgA is diagnostic; persistence of IgG beyond age 12 mo also diagnostic</li> <li>• Eye examination</li> <li>• Cerebral calcifications best seen on CT</li> </ul>	Pyrimethamine + sulfadiazine with folinic acid for at least 12 months
Syphilis*	Possible signs: hepatosplenomegaly, snuffles (copious nasal secretions), lymphadenopathy, mucocutaneous lesions, pneumonia, osteochondritis, hemolytic anemia, or thrombocytopenia. Skin lesions and secretions are highly infectious	<ul style="list-style-type: none"> <li>• All women should be screened prenatally</li> <li>• If maternal serology positive, screen infant using non-treponemal test such as VDRL or RPR</li> <li>• Confirmatory test using treponemal test such as FTA-ABS or MHA-TP.† See Table EC 17-A</li> </ul>	<p><b>For abnormal neonatal testing/physical examination:</b></p> <p>aqueous penicillin G, 50,000 U/kg IV Q12 hr (age 1 week or younger) or Q8 hr (&gt;age 1 week); <b>or</b> procaine penicillin G, 50,000 U/kg IM as a single daily dose for 10 days</p> <p><b>For normal neonatal tests:</b></p> <p>benzathine penicillin G, 50,000 U/kg IM, single dose</p>
Rubella*	IUGR, cataracts, cardiac anomalies, deafness, "blueberry muffin rash"	<ul style="list-style-type: none"> <li>• IgM positive at birth—3 months</li> <li>• Eye examination</li> <li>• Echocardiogram</li> </ul>	Supportive care for newborn Ensure mother is immunized
Cytomegalovirus (CMV)	90% asymptomatic at birth: IUGR, jaundice, hepatosplenomegaly, microcephaly, thrombocytopenia, intracranial calcifications, hearing loss	Virus can be isolated in cell culture from urine, stool, respiratory tract, CSF, peripheral blood leukocytes. Also can test IgM within 3 weeks of birth	Ganciclovir 6 mg/kg/dose IV Q12 hr for 6 weeks Valganciclovir 16 mg/kg/dose PO BID
Parvovirus B19	Fetal hydrops, IUGR, intellectual disability, isolated pleural and pericardial effusions; risk of fetal death when infection occurs during pregnancy is 2%–6%, greatest risk in first half of pregnancy	Positive serum IgM suggests infection occurred 2–4 months earlier	Supportive care

\*All mothers should be screened prenatally for rubella immune status and syphilis.

†Link to diagnostic algorithm for syphilis: <http://aapredbook.aappublications.org/content/1/SEC131/SEC268/F2192.large.jpg>.

‡See 2012 American Academy of Pediatrics *Red Book* for isolation recommendations.

BID, Twice daily; CSF, cerebrospinal fluid; CT, computed tomography; IM, intramuscular; IUGR, intrauterine growth retardation; IV, intravenous; FTA-ABS, fluorescent treponemal antibody absorption test; MHA-TP, microhemagglutination assay for *Treponema pallidum* antibodies; PO, oral; RPR, rapid plasma reagin; VDRL, Venereal Disease Research Laboratory test.

TABLE 17-8

## PERINATAL INFECTIONS

Infective Agent	Clinical Findings	Diagnostic Testing	Therapy
Herpes simplex virus (HSV)	HSV can present any time within the first 1–3 weeks of life as: 1. Disease localized to SEM. 2. Localized CNS infection. 3. Disseminated disease with severe pneumonitis and hepatitis Disseminated disease often presents in the first to second week of life; CNS disease presents later, often in the second to third week of life.	<ul style="list-style-type: none"> <li>• Surface culture: conjunctiva, nasopharynx, mouth, rectum, blood, CSF, skin vesicles</li> <li>• PCR: blood, CSF</li> <li>• Ancillary: CMP looking for elevated transaminase; CXR looking for pneumonitis</li> </ul>	Acyclovir 20 mg/kg/dose IV Q8 hr <ul style="list-style-type: none"> <li>• 14 days for skin, eye, and mouth disease</li> <li>• 21 days with up to 6 months prophylaxis for disseminated disease</li> </ul>
Varicella <sup>10</sup>	Maternal infection from 5 days prior or 2 days after delivery can result in severe neonatal infection in first 2 weeks. Can include pneumonitis, encephalitis, purpura fulminans, bleeding, death. Maternal infection >5 days before delivery and GA >28 weeks causes milder disease.	<ul style="list-style-type: none"> <li>• DFA of vesicle scraping</li> <li>• PCR from vesicle or CSF</li> </ul>	Infant: VariZIG and/or acyclovir if mother developed primary varicella (not zoster) between 5 days before and 2 days after delivery, and hospitalized preterm infants < 28 weeks or > 28 weeks if mother lacks historical or serologic evidence of protection.
Enterovirus	Neonates can develop severe infection: hepatitis, myocarditis, meningitis, encephalitis, pneumonitis, DIC.	RNA PCR from throat, stool, rectal swab, urine, blood, or CSF	IVIG
Hepatitis B virus (HBV) <sup>11</sup>	In utero transmission accounts for <2% of perinatal infections. If mother is both HBsAg positive and HBeAg positive, risk for development of chronic HBV infection is 70%–90% by age 6 months unless postexposure immunoprophylaxis is given. Risk is 5%–20% when mother is HBsAb positive and HBeAg negative. Appropriate prophylaxis is highly effective.	ALT is usually normal at birth, with detectable HBeAg and high HBV DNA concentrations ( $\geq 20,000$ IU/mL) Testing for HBsAg and anti-HBs should be done at 9 and 18 months in infants with HBsAg-positive mothers	Newborns of HBsAg-positive or unknown mothers should receive HBV vaccine and HBIG 0.5 mL IM within 12 hours of life. (See FIGURE 16-4: Management of neonates born to mothers with unknown or positive HBsAg status.) Breast-feeding not contraindicated

*Continued*

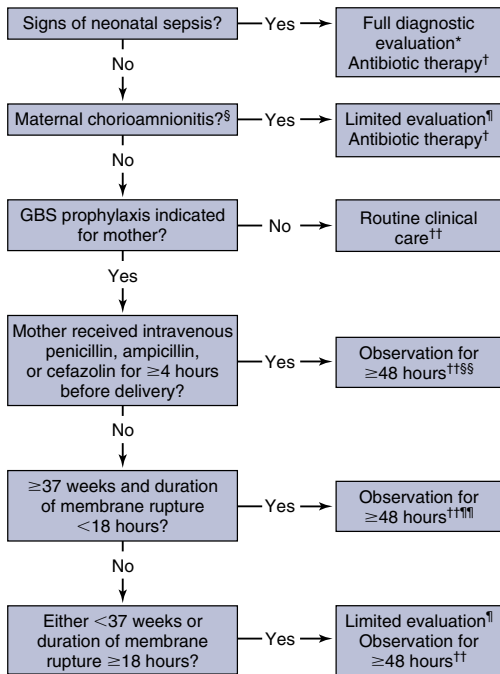
TABLE 17-8

## PERINATAL INFECTIONS (Continued)

Infective Agent	Clinical Findings	Diagnostic Testing	Therapy
Hepatitis C virus (HCV)	Risk of perinatal transmission is 5% and occurs only from women who are HCV RNA positive at time of delivery. Maternal co-infection with HIV is associated with increased risk of perinatal transmission.	HCV RNA can be detected in serum or plasma within 1–2 weeks after exposure and weeks before onset of liver enzyme abnormalities. Maternal anti-HCV antibodies can persist up to 18 months.	No therapy until HCV status ascertained. Nonpegylated interferon- $\alpha$ -2b plus ribavirin approved in children aged 3–17 years, but no data for neonates. Refer to pediatric hepatitis specialist. Breast-feeding not contraindicated.
Human immunodeficiency virus (HIV)*	Most mother-to-child transmission occurs perinatally, with lower rates of transmission occurring in utero and postnatally through breast-feeding. Risk factors for transmission: 1. Greater viral exposure, especially maternal viral load. 2. Risk increases with longer duration of ruptured membranes, more months of breast-feeding, vaginal delivery, or laboring before cesarean section.	<ul style="list-style-type: none"> <li>If high risk of acquiring infection (i.e., high maternal VL), HIV DNA PCR at 48–72 hours of life</li> <li>If lower risk, test at 2 weeks of life</li> </ul>	See Table 17-12 Breastfeeding contraindicated

ALT, Alanine aminotransferase; CMP, comprehensive metabolic panel; CNS, central nervous system; CSF, cerebrospinal fluid; CXR, chest x-ray; DFA, direct fluorescent antibody; DIC, disseminated intravascular coagulation; GA, gestational age; HBIG, hepatitis B immune globulin; IM, intramuscular; IV, intravenous; IVIG, intravenous immunoglobulin; PCR, polymerase chain reaction; sAb, surface antibody; sAg, surface antigen; SEM, skin, eyes, mouth; VL, viral load; VZIG, varicella-zoster immune globulin.

\*From Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to reduce perinatal HIV transmission in the United States. Available at <http://aidsinfo.nih.gov/contentfiles/vguidelines/PerinatalGL.pdf>. Tables 8 and 9. Accessed December 11, 2012.



\* Full diagnostic evaluation includes a blood culture, a complete blood count (CBC), including white blood cell differential and platelet counts, chest radiograph (if respiratory abnormalities are present), and lumbar puncture (if patient is stable enough to tolerate procedure and sepsis is suspected).

† Antibiotic therapy should be directed toward the most common causes of neonatal sepsis, including intravenous ampicillin for GBS and coverage for other organisms (including *Escherichia coli* and other gram-negative pathogens) and should take into account local antibiotic resistance patterns.

§ Consultation with obstetric providers is important to determine the level of clinical suspicion for chorioamnionitis. Chorioamnionitis is diagnosed clinically and some of the signs are nonspecific.

¶ Limited evaluation includes blood culture (at birth) and CBC with differential and platelets (at birth and/or at 6–12 hours of life).

†† If signs of sepsis develop, a full diagnostic evaluation should be conducted and antibiotic therapy initiated.

§§ If ≥37 weeks' gestation, observation may occur at home after 24 hours if other discharge criteria have been met, access to medical care is readily available, and a person who is able to comply fully with instructions for home observation will be present. If any of these conditions is not met, the infant should be observed in the hospital for at least 48 hours and until discharge criteria are achieved.

¶¶ Some experts recommend a CBC with differential and platelets at age 6–12 hours.

**FIGURE 17-3**

Algorithm for secondary prevention of early-onset group B streptococcal (GBS) disease among newborns. (From Verani JR, McGee L, Schrag SJ; Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention [CDC]. Prevention of perinatal group B streptococcal disease—revised guidelines from CDC, 2010. MMWR Recomm Rep. 2010;59:1-36.)

TABLE 17-9

## NEONATAL BACTERIAL INFECTIONS: GUIDELINES FOR INITIAL MANAGEMENT

Infectious Syndrome	Empirical Therapy	Comments
<b>Conjunctivitis</b>	Saline irrigation regardless of etiology	
<i>Chlamydia trachomatis</i>	Erythromycin 50 mg/kg/day PO/IV divided QID for 14 days <i>Alt: azithromycin for 5 days</i>	Exudative conjunctivitis. Onset 3–10 days. Topical treatment ineffective
<i>Neisseria gonorrhoeae</i>	Ceftriaxone 25–50 mg/kg IV/IM, single dose (max 125 mg) <i>Alt: cefotaxime, single dose</i>	Exudative conjunctivitis. Onset 2–4 days. Admit for evaluation and treatment of possible disseminated disease
<b>Meningitis</b>		
GBS, <i>Escherichia coli</i> , <i>Listeria monocytogenes</i>	Ampicillin + cefotaxime. Treat 14 days for GBS infection, 21 days for <i>Listeria</i> For gram-negative organisms: cefotaxime for 21 days	Gentamicin not recommended; poor CSF penetration
<b>Pneumonia</b>		
GBS, <i>Staphylococcus aureus</i> , <i>L. monocytogenes</i>	Ampicillin + gentamicin Consider vancomycin if MRSA prevalent Treat 10–21 days, depending on severity	Blood cultures indicated Effusions should be drained; Gram stain and culture collected on fluid
<i>C. trachomatis</i>	Erythromycin 50 mg/kg/day PO/IV divided QID for 14 days <i>Alt: azithromycin for 5 days</i>	Presents at 2–19 weeks of life with staccato cough, tachypnea, rales, bilateral infiltrates, and hyperinflation on CXR; usually afebrile
<b>Septic arthritis</b>		
<i>S. aureus</i> , GBS, gram-negative bacilli	(Cefotaxime or gentamicin) + (nafcillin or oxacillin if <i>S. aureus</i> suspected)	Drainage necessary
<b>Sepsis</b>	Ampicillin + (gentamicin or cefotaxime)	

First antibiotic listed indicates treatment of choice. Alternative regimens are listed in italics. Cultures should be obtained when clinically appropriate; antibiotic coverage should be narrowed when organism and susceptibility information is available.

Alt., Alternative; CSF, cerebrospinal fluid; CXR, chest x-ray; GBS, group B streptococcal; IM, intramuscular; IV, intravenous; MRSA, methicillin-resistant *Staphylococcus aureus*; PO, oral; QID, four times daily.

## C. Common Neonatal Bacterial Infections and Pediatric Infections: Guidelines for Initial Management (Table 17-9 and Table 17-10)

### D. Sexually Transmitted and Genitourinary Infections

#### 1. Common sexually transmitted infections (Table 17-11)

#### 2. Pelvic inflammatory disease:

- Differential diagnosis is broad and includes endometriosis, tubo-ovarian abscess, ovarian cyst, ectopic pregnancy, acute surgical abdomen, irritable bowel disease (IBD), pyelonephritis, dysmenorrhea, septic/threatened abortion.

TABLE 17-10

## COMMON PEDIATRIC INFECTIONS: GUIDELINES FOR INITIAL MANAGEMENT

Infectious Syndrome	Usual Etiology	Suggested Empirical Therapy	Suggested Length of Therapy/Comments
<b>Bites</b>			
Human	<i>Streptococcus</i> spp., <i>Staphylococcus aureus</i> , oral anaerobes, <i>Eikenella corrodens</i> , <i>Haemophilus</i> spp.	<b>PO:</b> amoxicillin/clavulanate <i>Alt:</i> clindamycin + (third-generation cephalosporin or TMP/SMX) <b>IV:</b> ampicillin/sulbactam <i>Alt:</i> TMP/SMX + clindamycin	For all bites, cleaning, irrigation, and débridement are critical. Human: 5–7 days. Assess immunization status (tetanus, hepatitis B) and HIV risk.
Dog/cat	Add <i>Pasteurella multocida</i> , <i>Streptococcus</i> spp., <i>Capnocytophaga</i> , oral anaerobes	Same	Animal: 7–10 days Assess tetanus immunization status, risk of rabies.
<b>Catheter-related blood-stream infections</b>	<i>S. aureus</i> , CoNS, enteric Gram-negative bacilli including <i>Pseudomonas</i> , <i>Candida</i> spp.	Immunocompetent: vancomycin + third-generation cephalosporin Immunocompromised: vancomycin + (cefepime or piperacillin/tazobactam)	Consider catheter removal and fungal coverage as clinically indicated.
<b>Cellulitis</b>	GAS, <i>S. aureus</i> (MSSA or MRSA)	<b>PO:</b> cephalexin; <i>clindamycin if MRSA prevalence high</i> <b>IV:</b> oxacillin; <i>clindamycin or vancomycin if MRSA prevalence high</i> TMP/SMX is not active against GAS	5 days Incision and drainage alone may be adequate and should be performed when indicated; obtain cultures for susceptibility. Hospitalize for severe infections, limb-threatening infections, immunocompromised status.
<b>Conjunctivitis</b> (suppurative, non-neonatal)	<i>Streptococcus pneumoniae</i> , <i>Haemophilus influenzae</i> (nontypeable), <i>Moraxella</i> , viral <i>Neisseria gonorrhoeae</i>	Ophthalmic erythromycin, bacitracin/polymyxin B, or polymyxin B/TMP Ceftriaxone IM	5 days Ointments preferred for infants or young children. Single dose. Consider <i>Chlamydia</i> treatment as clinically indicated.
<b>Dacrocystitis</b>	<i>S. pneumoniae</i> , <i>H. influenzae</i> , <i>S. aureus</i> , <i>Streptococcus pyogenes</i> , <i>Pseudomonas aeruginosa</i>	Initial management: warm compresses PO: oxacillin or cephalexin	Consider ophthalmologic evaluation to relieve obstruction.

TABLE 17-10

## COMMON PEDIATRIC INFECTIONS: GUIDELINES FOR INITIAL MANAGEMENT (Continued)

Infectious Syndrome	Usual Etiology	Suggested Empirical Therapy	Suggested Length of Therapy/Comments
Dental abscesses	Oral flora, including anaerobes	Clindamycin or amoxicillin/clavulanic acid	Consider dental evaluation for surgical drainage.
Gastroenteritis (Bacterial)	<i>Escherichia coli</i>	Antibiotics strongly discouraged because of possible increased risk of HUS occurring in patients with <i>E. coli</i> O157:H7 treated with antibiotics <sup>12</sup>	
	<i>Salmonella</i> spp.	Azithromycin or ciprofloxacin for traveler's diarrhea Ceftriaxone <i>Alt: azithromycin, ampicillin, amoxicillin, or TMP/SMX for susceptible strains</i>	10–14 days for infants <age 3 months, bacteremia, toxic appearance, hemoglobinopathy, or immunosuppressed. Antibiotics generally not indicated otherwise.
	<i>Shigella</i> spp.	Ceftriaxone, azithromycin, or fluoroquinolone	5 days for dysentery, immunosuppressed, or to prevent spread in mild disease. Oral cephalosporins not useful. High rates resistance with amoxicillin or TMP/SMX.
	<i>Yersinia</i> spp.	TMP/SMX, aminoglycosides, cefotaxime, fluoroquinolone, or tetracycline	Usually no antibiotic therapy is recommended except with bacteremia, extraintestinal infections, or immunocompromised hosts.
	<i>Campylobacter</i> spp. <i>Clostridium difficile</i>	Azithromycin or erythromycin Metronidazole Oral vancomycin for severe infection	5–7 days; shortens duration of fecal shedding 10 days Stop the precipitating antibiotic therapy
Influenza	Influenza A and B	Recommendations vary yearly based on characteristics and resistance patterns	See <a href="http://www.cdc.gov/flu/">http://www.cdc.gov/flu/</a> for most up-to-date recommendations.



TABLE 17-10

## COMMON PEDIATRIC INFECTIONS: GUIDELINES FOR INITIAL MANAGEMENT (Continued)

Infectious Syndrome	Usual Etiology	Suggested Empirical Therapy	Suggested Length of Therapy/Comments
<b>Intraabdominal infections</b>	<i>E. coli</i> , <i>Enterococcus</i> , <i>Bacteroides</i> spp., <i>Clostridium</i> spp., <i>Peptostreptococcus</i> , <i>P. aeruginosa</i> , <i>S. aureus</i> , other Gram-negative bacilli	<b>Single agent:</b> piperacillin-tazobactam, ticarcillin-clavulanate <b>Combo:</b> (ceftriaxone or cefepime) + metronidazole	4–7 days For patients with health care–associated infection, consider MRSA coverage.
<b>Lymphadenitis</b>	Viruses, GAS, <i>S. aureus</i> , anaerobes, atypical mycobacteria, <i>Actinomyces</i> , <i>Bartonella henselae</i> (cat scratch disease), <i>Mycobacterium tuberculosis</i>	<b>PO:</b> amoxicillin/clavulanate; clindamycin if MRSA prevalent <i>Alt:</i> cephalexin or dicloxacillin <b>IV:</b> oxacillin or cefazolin; clindamycin if MRSA prevalent	Surgical excision with <i>M. tuberculosis</i> , atypical mycobacteria. Needle aspiration with <i>B. henselae</i> . If allergic to PCN: cefdinir, cefuroxime, or vancomycin
<b>Mastoiditis (acute)</b>	<i>S. pneumoniae</i> , <i>S. pyogenes</i> , <i>S. aureus</i> , <i>H. influenzae</i> (nontypeable)	Third-generation cephalosporin	4 weeks Surgical management required; definitive therapy should be guided by culture obtained at surgery.
<b>Meningitis (non-neonatal)</b> age > 1 month	<i>S. pneumoniae</i> , <i>Neisseria meningitidis</i> , <i>H. influenzae</i>	Ceftriaxone + vancomycin For severe PCN allergy, consider chloramphenicol + vancomycin or levofloxacin	Duration depends on organism. See <i>Red Book: 2012</i> <sup>9</sup> for chemoprophylaxis recommendations for contacts of meningococcal and Hib disease. Dexamethasone use, except for with <i>H. influenzae</i> , is controversial.
<b>Orbital cellulitis</b>	<i>S. pneumoniae</i> , <i>H. influenzae</i> (nontypeable), <i>Moraxella catarrhalis</i> , <i>S. aureus</i> , GAS	Ampicillin/sulbactam; OR (cefotaxime or ceftriaxone) AND (clindamycin or vancomycin or oxacillin)	10 days Recommend ophthalmologic consultation; CT to evaluate intracranial extension.

Continued

TABLE 17-10

## COMMON PEDIATRIC INFECTIONS: GUIDELINES FOR INITIAL MANAGEMENT (Continued)

Infectious Syndrome	Usual Etiology	Suggested Empirical Therapy	Suggested Length of Therapy/Comments
<b>Osteomyelitis</b>			
Uncomplicated	<i>S. aureus</i> , GAS, <i>Streptococcus</i> spp., <i>Kingella kingae</i> ( $\leq 4$ years)	Oxacillin, nafcillin, or clindamycin <i>Alt: TMP-SMX</i>	4–6 weeks Clindamycin ineffective as monotherapy for <i>Kingella</i> .
Foot puncture	Add <i>P. aeruginosa</i> coverage	Add ceftazidime or antipseudomonal PCN	
Sickle cell disease	Add <i>Salmonella</i> spp. coverage	Add ceftriaxone	
<b>Otitis media (acute)</b> <sup>13</sup>	<i>S. pneumoniae</i> , <i>H. influenzae</i> (nontypeable), <i>M. catarrhalis</i>	High dose Amoxicillin 80-90 mg/kg/day If child has received Amoxicillin within the past 30 days or has concurrent purulent conjunctivitis, Amoxicillin-Clavulanate is recommended <i>Alt/PCN Allergy: Cefdinir, Cefpodoxime, Ceftriaxone</i> For treatment failure (persistent symptoms 48-72 hours after initial treatment): Amoxicillin-Clavulanate or Ceftriaxone (IM daily x 3 days) <i>Alt: Clindamycin + 3rd generation cephalosporin</i>	10 days for children age < 2 years and all children with severe symptoms 7 days for children ages 2-5 years with mild-moderate symptoms 5-7 days for children > age 6 years with mild-moderate symptoms Consider watchful waiting in patients 6-23 months with unilateral, nonsevere symptoms or in patients > 2 years with nonsevere symptoms Consider tympanocentesis and specialist consultations
<b>Otitis externa (uncomplicated)</b>	<i>Pseudomonas</i>	Eardrops: ciprofloxacin	7–10 days Analgesics for pain
<b>Parotitis</b>	<i>S. aureus</i> most common; also oral flora, gram-negative rods, viruses (including mumps, HIV, EBV), or noninfectious causes	PO: clindamycin or nafcillin/oxacillin or amoxicillin/clavulanic acid	Sialogogues, local heat, gentle massage of gland from posterior to anterior, and hydration provide symptomatic relief. Surgical drainage may be required. Consider HIV test if chronic parotitis.

TABLE 17-10

## COMMON PEDIATRIC INFECTIONS: GUIDELINES FOR INITIAL MANAGEMENT (Continued)

Infectious Syndrome	Usual Etiology	Suggested Empirical Therapy	Suggested Length of Therapy/Comments
Periorbital cellulitis (preseptal)	GAS and <i>Streptococcus</i> spp., <i>S. aureus</i> , <i>H. influenzae</i> (nontypeable), <i>M. catarrhalis</i>	Ampicillin/sulbactam or amoxicillin/clavulanic acid or third-generation cephalosporin Consider adding vancomycin, TMP/SMX, or clindamycin if concern for MRSA	10–14 days If secondary to local trauma and not associated with sinusitis, treat as staph/strep cellulitis.
Pertussis	<i>Bordetella pertussis</i>	Azithromycin, erythromycin Azithromycin for age < 1 month	5 days for Azithromycin. 10 days for Erythromycin Chemoprophylaxis for close contacts
Pharyngitis	GAS, group C and G streptococci, <i>Arcanobacterium haemolyticum</i> , viruses (including coxsackievirus, other enteroviruses, EBV)	PCN V or amoxicillin Benzathine PCN G × 1 for GAS <i>Alt: clindamycin, macrolide, or cephalexin</i>	10 days (to prevent acute rheumatic fever in GAS infection). Supportive treatment only for viral pharyngitis.
<b>Pneumonia (non-neonatal)</b>			
Age < 5 years	<i>S. pneumoniae</i> , <i>Mycoplasma</i> , <i>Chlamydia pneumoniae</i> , GAS, <i>S. aureus</i> , viruses, influenza	<b>Outpatient:</b> amoxicillin (high-dose), ± azithromycin (atypical coverage) <i>Alt: clindamycin</i> <b>Inpatient:</b> ampicillin ± azithromycin <i>Alt: ceftriaxone + azithromycin</i>	10 days Atypical organisms ( <i>Mycoplasma</i> , <i>Chlamydia</i> ) are more likely in children > age 5 years. Add vancomycin or clindamycin if severe illness or features suggestive of <i>S. aureus</i> (pleural effusion, cavitation).
Age > 5 years (and immunized)	<i>S. pneumoniae</i> , <i>Mycoplasma</i> , <i>C. pneumoniae</i> , GAS, <i>S. aureus</i> , viruses, influenza	<b>Outpatient:</b> azithromycin ± amoxicillin (high dose) <i>Alt: azithromycin ± clindamycin</i> <b>Inpatient:</b> ampicillin + azithromycin <i>Alt: ceftriaxone or cefotaxime + azithromycin</i>	7–10 days Vancomycin or clindamycin if severe illness or features suggestive of <i>S. aureus</i> (pleural effusion, cavitation).

Continued

TABLE 17-10

## COMMON PEDIATRIC INFECTIONS: GUIDELINES FOR INITIAL MANAGEMENT (Continued)

Infectious Syndrome	Usual Etiology	Suggested Empirical Therapy	Suggested Length of Therapy/Comments
Nonimmunized child (for <i>H. influenzae</i> , <i>S. pneumoniae</i> )	See above	Ceftriaxone or cefotaxime ± azithromycin	Consider vancomycin or clindamycin for MRSA coverage.
<b>Spinal fusion infections</b>	<i>Staphylococcus</i> , <i>Streptococcus</i> spp.; enteric or genitourinary Gram-negative organisms	Vancomycin + piperacillin/tazobactam	Greater than 3 months Consider washout of wound initially. Deep tissue culture of wound may direct treatment. Removal of instrumentation may be necessary.
<b>Septic arthritis (non- neonatal)</b>			
Age < 5 years	<i>S. aureus</i> , GAS, <i>S. pneumoniae</i> , <i>Kingella kingae</i> (≤4 years)	Clindamycin or oxacillin. Add amoxicillin for <i>Kingella</i>	3 weeks (IV) Aspiration of affected joint recommended. May switch to PO after response.
Age > 5 years	<i>S. aureus</i> , GAS, <i>Streptococcus</i> spp.	Nafcillin, oxacillin, or clindamycin <i>Alt: vancomycin</i>	
Adolescent	Add <i>N. gonorrhoeae</i>	Add ceftriaxone	
<b>Sinusitis<sup>20</sup></b>			
Acute	<i>S. pneumoniae</i> , <i>H. influenzae</i> , <i>M. catarrhalis</i>	Amoxicillin/clavulanate <i>Alt: cefpodoxime or cefixime</i> If PCN allergy: levofloxacin If no improvement in 3–5 days, broaden coverage	10 days If severe/fails to respond, consider imaging and/or drainage.
Chronic	Add <i>S. aureus</i> , anaerobes	Amoxicillin/clavulanic acid, cefpodoxime, cefurox- ime, or cefdinir <i>Alt: fluoroquinolone</i>	7 days after resolution of symptoms.
Seriously ill or immuno- compromised	Add <i>Pseudomonas</i> , gram-negative bacilli, <i>Mucor</i> , <i>Rhizopus</i> , <i>Aspergillus</i>	Cefepime or piperacillin/tazobactam ± amphi- tericin B	Surgical intervention needed.

TABLE 17-10

## COMMON PEDIATRIC INFECTIONS: GUIDELINES FOR INITIAL MANAGEMENT (Continued)

Infectious Syndrome	Usual Etiology	Suggested Empirical Therapy	Suggested Length of Therapy/Comments
Tracheitis	<i>S. aureus</i> , <i>S. pneumoniae</i> , GAS, <i>M. catarrhalis</i> , <i>H. influenzae</i> , <i>Pseudomonas</i>	Ceftriaxone + clindamycin if community-acquired Cefepime or piperacillin-tazobactam if ventilator or tracheostomy dependent	5 days
UTI			
Cystitis	<i>E. coli</i> , Enterobacteriaceae, <i>Proteus</i> spp., <i>Staphylococcus saprophyticus</i> , <i>Enterococcus</i> spp.	<b>PO:</b> TMP/SMX, cefixime <b>IV:</b> cefotaxime or ceftriaxone <i>OR</i> ampicillin and gentamicin <i>Alt:</i> nitrofurantoin or ciprofloxacin	7–14 days Consider phenazopyridine for comfort (urine and other secretions may turn red). For severe PCN allergy or resistant organisms.
Pyelonephritis	<i>E. coli</i> , Enterobacteriaceae, <i>Proteus</i> spp., <i>Enterococcus</i> spp.	Ceftriaxone <i>OR</i> ampicillin + gentamicin <i>Alt:</i> cefixime or ciprofloxacin	7–14 days Outpatient treatment if well appearing. Consider initial dose of parenteral therapy.
Abnormal host/urinary tract	Add <i>Pseudomonas</i> , resistant gram-negative organisms	Piperacillin/tazobactam or cefepime	7–14 days
Ventriculoperitoneal shunt, infected	<i>S. epidermidis</i> , <i>S. aureus</i> , Enterobacteriaceae, <i>Propionibacterium acnes</i>	Vancomycin + cefepime	10–21 days, depending on organism and response. Shunt removal or revision is often required for successful treatment.

First antibiotics listed indicate treatment of choice. *Alternative treatment regimens are listed in italics.* Cultures should be obtained when clinically appropriate; antibiotic coverage should be narrowed once organism and susceptibility information is available.

CoNS, Coagulase-negative staphylococci; CT, computed tomography; CXR, chest x-ray; EBV, Epstein-Barr virus; FDA, U.S. Food and Drug Administration; GAS, group A streptococcus; GBS, group B streptococcus; Hib, *Haemophilus influenzae* type b; HIV, human immunodeficiency virus; IM, intramuscular; IV, intravenous; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*; PCN, penicillin; PO, by mouth; TMP/SMX, trimethoprim/sulfamethoxazole; UTI, urinary tract infection.

Recommendations modified from American Academy of Pediatrics. Pickering LK, Baker CJ, Kimberlin DW, Long SS, eds. *Red Book: 2012 Report of the Committee on Infectious Diseases*. 29th ed. Elk Grove Village, Ill: AAP, 2012; and McMillan JA, Siberry GK, Dick JD, et al. *The Harriet Lane Handbook of Pediatric Antimicrobial Therapy*. Philadelphia: Mosby Elsevier, 2009.

TABLE 17-11

## SEXUALLY TRANSMITTED AND GENITOURINARY INFECTIONS: GUIDELINES FOR MANAGEMENT

Infection	Clinical Diagnosis	Empirical Therapy	Comments
<b>Bacterial vaginosis</b>		Metronidazole 500 mg PO BID OR Metronidazole Gel 0.75% (5 g) intravaginally daily OR Clindamycin Cream 2% 5 g intravaginally	7 days 5 days 7 days
<b>Chlamydia infections</b>	Uncomplicated urethritis, endocervicitis, or proctitis	Azithromycin 1 g PO once OR Doxycycline 100 mg PO BID for 7 days <i>Alt: erythromycin PO QID or fluoroquinolone for 7 days</i>	Consider empirical treatment for gonorrhea secondary to common co-infection. See below for instructions for therapy for sexual partners.
	Chlamydia infection in pregnancy	Azithromycin 1 g PO once Amoxicillin 500 mg PO TID for 7 days Erythromycin PO QID for 7 days	Repeat testing (3 weeks posttreatment) to document chlamydial eradication is in all pregnant patients.
<b>Gonorrhea infections</b>	Uncomplicated infection of the cervix, urethra, rectum, or pharynx	Ceftriaxone 250 mg IM once, <b>PLUS</b> Azithromycin 1 g PO once	Dual treatment is recommended for gonorrhea secondary to organism resistance.
	Epididymitis	Ceftriaxone 250 mg IM once, <b>PLUS</b> Doxycycline 100 mg PO BID for 10 days	For MSM, add a fluoroquinolone for 10 days.
	Disseminated gonococcal infections	Ceftriaxone 1 g IV/IM daily <i>Alt: cefotaxime 1g IV q8 hours</i>	Can switch to cefixime 400 mg PO BID 24–48 hours after clinical improvement. Total therapy course: 7 days.
<b>Pelvic inflammatory disease</b>	See Chapter 17 Section II.D.2.C	<b>Outpatient:</b> ceftriaxone 250 mg IM once, <b>PLUS</b> Doxycycline 100 mg PO BID for 14 days ± metronidazole 500 mg PO BID x 14 days  <b>Inpatient: regimen A</b> (2g Cefotetan IV Q12 hr OR 2g Cefoxitin IV Q6 hr) plus doxycycline 100 mg IV Q12 hr <b>Regimen B:</b> clindamycin 900 mg IV Q8 hr plus gentamicin 2 mg/kg loading dose, then 1.5 mg/kg IV Q8 hr maintenance (or single daily dosing)	Switch to oral therapy 24 hours after clinical improvement to complete 14 days of treatment with doxycycline BID or clindamycin QID.
<b>Syphilis</b>	Primary, secondary, or early latent syphilis (<1 year duration)	Benzathine PCN G 50,000 U/kg (max 2.4 million units) IM (single dose) <i>Alt: doxycycline 100 mg PO BID for 14 days OR tetracycline 500 mg PO QID for 14 days</i>	Data is limited for penicillin alternatives

TABLE 17-11

**SEXUALLY TRANSMITTED INFECTIONS: GUIDELINES FOR MANAGEMENT (Continued)**

Infection	Clinical Diagnosis	Empirical Therapy	Comments
	Late syphilis (>1 year duration); tertiary syphilis	Benzathine PCN G 50,000 U/kg (max 2.4 million units) IM Q1 week for 3 weeks <i>Alt: doxycycline 100 mg PO BID for 28 days OR tetracycline 500 mg PO QID for 28 days</i>	
	Neurosyphilis	See formulary for dosing	
Trichomonas		Metronidazole 2 g PO once	Refer partner for testing and treatment.
Herpes (genital, non-neonatal)		Acyclovir or Valacyclovir	See formulary for treatment for initial infection and recurrence
Candidiasis (Vulvovaginal)		Fluconazole PO OR intravaginal cream	See formulary

PCN G, penicillin G.

Patients should be instructed to refer their partners for diagnosis, testing, and treatment. For dosing for children ≤8 years of age or <45 kg or for additional alternative regimens, please refer to the CDC Treatment Guidelines, 2010: <http://www.cdc.gov/std/treatment/2010/>.

- b. Workup: Pelvic and bimanual examination, gonorrhea/chlamydia (GC/CT) testing, HIV, human chorionic gonadotropin (hCG), wet preparation, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and urinalysis/urine culture (UA/UCx) if clinically indicated. Consider a complete blood cell count (CBC) with differential and pelvic ultrasound if the patient is ill-appearing, has an adnexal mass on bimanual examination, or is not improving after antibiotics.
- c. Minimum diagnostic criteria: Uterine, adnexal, or cervical motion tenderness without other identifiable causes. One or more of the following additional criteria enhances specificity: fever ( $>38.3^{\circ}\text{C}$ ), mucopurulent vaginal or cervical discharge, leukocytes on saline microscopy, increased ESR or CRP, laboratory documentation of chlamydial or gonorrhea infection.
- d. Treatment: Empirical treatment is indicated for all sexually active females if minimum diagnostic criteria are met and no other cause for symptoms is identified. See Table 17-11 and the Centers for Disease Control and Prevention (CDC) STD Treatment Guidelines for most up-to-date information (<http://www.cdc.gov/std/treatment/2010/pid.htm>).
- e. Admission criteria: Cannot exclude acute surgical abdomen, presence of tubo-ovarian abscess, pregnancy, immunodeficiency, severe illness (nausea, vomiting, anorexia), inability to tolerate or follow outpatient oral regimen, failure to respond to appropriate outpatient therapy, follow-up cannot be ensured.

**E. Human Immunodeficiency Virus and Acquired Immunodeficiency Syndrome**

Recommendations provided are current at the time of publication. Please see the CDC guidelines on the diagnosis and management of children

with HIV infection at [www.aidsinfo.nih.gov/](http://www.aidsinfo.nih.gov/) for the most up-to-date recommendations.

1. **Counseling and testing:** Legal requirements for consent vary by state.

Counseling includes informed consent for testing, implications of positive test results, and prevention of transmission:

a. Prenatal testing:

(1) CDC guidelines state that HIV screening should be included in the routine panel of prenatal tests for all pregnant women, on an opt-out basis, after notifying the patient that testing will be conducted.<sup>14</sup>

(2) CDC also recommends that repeat HIV antibody testing occur in the third trimester, preferably before 36 weeks of gestation.<sup>14</sup>

b. Perinatal and newborn testing:

(1) For women in labor with undocumented HIV infection status during pregnancy or for infants born to mothers with unknown HIV status, a rapid HIV test should be performed on the mother on an opt-out basis.

(2) If an HIV rapid antibody test is positive, confirmatory testing (e.g., Western blot) should be pursued. If confirmatory testing is positive, virologic testing (HIV DNA polymerase chain reaction (PCR) or HIV RNA assay) should be completed.

c. Adolescent testing: CDC recommends HIV screening with opt-out consent as part of routine clinical care in all healthcare settings for patients, beginning at age 13 years. Repeat HIV-1 antibody testing should be performed on a regular basis for adolescents who remain at risk of HIV-1 infection. When there is suspicion for recent exposure, virologic testing should be pursued.

2. **Management of perinatal HIV exposure<sup>14,15</sup>:** Recommendations provided are current at the time of publication; check the recent recommendations for most current therapy at [www.aidsinfo.nih.gov/](http://www.aidsinfo.nih.gov/):

a. Prevention of mother-to-child transmission<sup>16</sup>: Three interventions are recommended to reduce transmission, including use of antiretroviral therapy during pregnancy, during delivery, and in the newborn; elective cesarean section for women with viral load >1000 copies/mL; and use of breast-feeding alternatives where they are found to be affordable, feasible, acceptable, sustainable, and safe. Healthcare professionals who are treating HIV-infected pregnant women and their newborn infants should report all instances of prenatal exposure to antiretroviral drugs (ARVs) to the Antiretroviral Pregnancy Registry (1-800-258-4263 or [www.apregistry.com](http://www.apregistry.com)):

(1) Pregnancy: Current guidelines recommend use of three-drug regimens during pregnancy and labor for all pregnant women with HIV infection. Zidovudine (ZDV) should be included in the pregnant woman's regimen (initiated at 14–34 weeks' gestation), because it has been shown to significantly reduce vertical transmission of HIV in combination with postnatal ZDV to the infant (Table 17-12). Elective cesarean section is recommended if possible at 38 weeks for all HIV-infected pregnant women with viral load >1000 copies/mL at time of delivery or who have unknown viral load. In the United



TABLE 17-12

## DIAGNOSIS AND MANAGEMENT FOR INFANTS WITH IN UTERO HIV EXPOSURE

Age	Laboratory Tests to Obtain*	Management	Comments
Newborn	(1) HIV DNA PCR if maternal status unknown and preliminary testing positive. Umbilical cord blood should not be used, owing to possible contamination with maternal blood. (2) Baseline CBC with differential.	(1) Start ZDV 4 mg/kg/dose PO BID, or 3 mg/kg IV Q12 hr within 12 hours of delivery. (2) Nevirapine if no maternal ARV: three doses at 12 mg/dose; first dose within 48 hours of birth, second dose 48 hours after first dose, third dose 96 hours after second dose.	Lower dose of ZDV for premature (<35 weeks GA) infants. Lower dose of nevirapine for infants <2 kg; concern for bone marrow suppression.
2–3 weeks	(1) HIV DNA PCR (or RNA assay)—consent signed if no prior consent for testing on chart (2) CBC with differential.	Check ZDV dosing and administration. Assess psychosocial needs, consider case management referral.	HIV antibody testing is not routine—only if lacking evidence of maternal HIV status (otherwise, antibody is expected to be positive in HIV-exposed infants).
4–6 weeks	(1) HIV DNA PCR (or RNA assay)—consent signed if no prior consent for testing on chart. (2) CBC with differential (use discretion, based on results of previous CBC).	(1) Discontinue ZDV regardless of PCR result (ZDV monotherapy is used during first 6 weeks for prophylaxis only). (2) Presumptively exclude HIV infection if results of $\geq 2$ weeks PCR and $\geq 4$ weeks PCR both negative. No TMP-SMX needed. (3) If PCR results not yet known, begin TMP-SMX at 75 mg/m <sup>2</sup> /dose BID for 3 consecutive days of week.	(1) If TMP-SMX is not tolerated, alternatives are aerosolized pentamidine, dapsone, or atovaquone (see Table EC 17-Bon Expert Consult for dosing guidelines). (2) TMP-SMX can be discontinued as soon as results of both $\geq 2$ weeks PCR and $\geq 4$ weeks PCR are negative. (3) <b>NOTE:</b> One single HIV-1 DNA PCR test has a sensitivity of 95% and a specificity of 97% for samples collected from infected infants 1 to 36 months of age.
2 months		(1) Check TMP-SMX dosing and administration if still needed. (2) Discontinue TMP-SMX if meets criteria above for negative testing.	Routine well-child check and immunizations.

Continued

TABLE 17-12

**DIAGNOSIS AND MANAGEMENT FOR INFANTS WITH IN UTERO HIV EXPOSURE (Continued)**

Age	Laboratory Tests to Obtain*	Management	Comments
4 months	HIV DNA PCR (or RNA assay).	Definitively exclude HIV infection: two negative PCRs (one $\geq 1$ month, one $\geq 4$ months) as long as no signs/symptoms of HIV infection.	(1) HIV is diagnosed (infected child) if any two separate DNA PCR assay results are positive. (2) If HIV infection is definitively excluded, infant needs only routine comprehensive well-child care, including all routine immunizations.
12, 15, 18 months	HIV antibody optional (to document clearance of maternal antibody—usually by 12 months but may persist to 18 months).		(1) Routine TB risk assessment, especially if HIV-infected household contacts, to determine need for PPD. (2) Routine well-child care and immunizations including MMR and varicella.

\*Any abnormal result requires prompt pediatric HIV specialist consultation.

ARV, Antiretroviral drug; CBC, complete blood cell count; GA, gestational age; MMR, measles/mumps/rubella; PCR, polymerase chain reaction; PPD, purified protein derivative; TB, tuberculosis; TMP-SMX, trimethoprim-sulfamethoxazole; ZDV, zidovudine.

Modified from Department of Health and Human Services guidelines for pediatric and perinatal HIV infection (see [www.aidsinfo.nih.gov](http://www.aidsinfo.nih.gov) for more detailed information). Accessed January 24, 2013.

States, current recommendations are that HIV-infected women should not breast feed.

- (2) Labor: For women with undetermined HIV status who are found to be positive on HIV rapid antibody test, antiretroviral prophylaxis should be administered to both mother and newborn without waiting for results of confirmatory HIV testing. If confirmatory test results are negative, prophylaxis may be discontinued and breast-feeding initiated.
- (3) Newborn: Oral administration of ZDV at 4 mg/kg/dose BID, beginning as soon as possible after birth and continuing for the first 6 weeks of life. If the mother received no prenatal ARVs, the infant should also be treated with nevirapine (three doses) in the first week of life (see Table 17-8 or Table 17-12). If infant prophylaxis with antiretrovirals in addition to ZDV is being considered, choice of drugs should be determined in consultation with an expert in pediatric HIV infection. Monitor ZDV toxicity with periodic CBC with differential count. Main toxicities are anemia and neutropenia. Consultation with an expert in pediatric HIV infection is advised if discontinuation of antiretrovirals is considered because of toxicity.

Exclusion of HIV infection is based on two negative antibody tests on different specimens after 6 months of age, or two negative virologic tests, one after 1 month of age and another after 4 months of age.

### 3. **Diagnosis and management of HIV-exposed infants (Table 17-12)**<sup>17</sup>

#### 4. **Opportunistic infections:**

- a. *Pneumocystis jiroveci* pneumonia (PCP) is the most common of the opportunistic infections. Trimethoprim-sulfamethoxazole (TMP-SMX) is recommended for all HIV-exposed infants until HIV infection is reasonably excluded, for all HIV-infected infants until age 12 months and for HIV-infected children and adolescents older than 1 year whose CD4 values fall into the severe immune suppression category (CD4 percentage < 15% or CD4 count < 200 cells/mm<sup>3</sup>)<sup>17</sup>
- b. For more detailed information, see Table EC 17-B on Expert Consult. Drug regimens for prevention and treatment of opportunistic infection in HIV infected children are given.

#### 5. **Management of HIV-infected infants and children**

Treatment guidelines change frequently; it is important to reference the most up-to-date guidelines at <http://www.aidsinfo.nih.gov/>:

- a. Criteria for initiation of antiretroviral therapy (ART)<sup>8</sup>:
  - (1) <12 months: All HIV-infected infants <age 12 months, regardless of immunologic, virologic, or clinical status should receive antiretroviral therapy.
  - (2) >12 months–3 years: Asymptomatic patients with CD4 cell count <1000 cells/mm<sup>3</sup> or CD4 percentage <25% should initiate ART.
  - (3) >3 years–5 years: Asymptomatic patients with CD4 cell count <750 cells/mm<sup>3</sup> or CD4 percentage <25% should initiate ART.
  - (4) 5 years and up: Asymptomatic patients with CD4 cell count <500 cells/mm<sup>3</sup> or CD4 percentage <25%.

TABLE EC 17-B

## DRUG REGIMENS FOR PREVENTION AND TREATMENT OF OPPORTUNISTIC DISEASE IN HIV-INFECTED INFANTS AND CHILDREN

Pathogen	Indication	Preventive Regimens	
		First Choice	Alternative
STRONGLY RECOMMENDED AS STANDARD OF CARE			
<i>Pneumocystis jiroveci</i> (formerly <i>Pneumocystis carinii</i> )	HIV-exposed infants 4–6 wk to 4 mo of age, HIV indeterminate or HIV-infected infants 4 mo to 12 mo of age; HIV-infected children 1–5 yr with CD4 count <500 $\mu$ L or CD4 percent <15%; HIV-infected children 6–12 yr with CD4 count <200 $\mu$ L or CD4 percent <15%	TMP/SMX 150/750 mg/m <sup>2</sup> /day in two divided doses PO 3 times/wk on consecutive days Acceptable alternative dosage schedules: <ul style="list-style-type: none"><li>• Single dose PO 3 times/wk on consecutive days</li><li>• Two divided doses PO every day</li><li>• Two divided doses PO 3 times/wk on alternate days</li></ul>	Aerosolized pentamidine (children $\geq$ 5 yr) 300 mg via Respigard II inhaler monthly; dapsone (children $\geq$ 1 mo) 2 mg/kg (max 100 mg) PO every day or 4 mg/kg (max 200 mg) PO every week Atovaquone (1–3 mo and >24 mo) 30 mg/kg daily; (4–24 mo) 45 mg/kg daily *If alternatives not tolerated, some clinicians use IV pentamidine (4 mg/kg)Q2–4 wk
<i>Mycobacterium tuberculosis</i>			
Isoniazid-sensitive	Tuberculin skin test (TST) reaction $\geq$ 5 mm or prior positive TST result without treatment or contact with case of active tuberculosis Tubercular disease must be excluded before start of treatment	Isoniazid 10–15 mg/kg (max 300 mg) PO every day $\times$ 9 mo or 20–30 mg/kg (max 900 mg) PO biweekly $\times$ 9 mo	Rifampin 10–20 mg/kg (max 600 mg) PO every day $\times$ 4–6 mo
Isoniazid-resistant	Same as for previous entry; high probability of exposure to isoniazid-resistant tuberculosis	Rifampin 10–20 mg/kg (max 600 mg) PO every day $\times$ 4–6 mo	Uncertain
Multidrug (isoniazid and rifampin)-resistant	Same as for previous entry; high probability of exposure to multidrug-resistant tuberculosis	Choice of drug requires consultation with public health authorities and depends on susceptibility of isolate from source patient	None

Continued

TABLE EC 17-B

## DRUG REGIMENS FOR PREVENTION AND TREATMENT OF OPPORTUNISTIC DISEASE IN HIV-INFECTED INFANTS AND CHILDREN (Continued)

Pathogen	Indication	Preventive Regimens	
		First Choice	Alternative
<i>Mycobacterium avium</i> complex	For children: <1 yr, CD4+ count < 750/ $\mu$ L 1–2 yr, CD4+ count < 500/ $\mu$ L 2–5 yr, CD4+ count < 75/ $\mu$ L 6 yr or older, CD4+ count < 50/ $\mu$ L	Clarithromycin 7.5 mg/kg (maximum 500 mg) PO BID <b>OR</b> azithromycin 20 mg/kg (max 1200 mg) PO once weekly	Azithromycin 5 mg/kg (max 250 mg) PO every day Children $\geq$ 6 yr: rifabutin 300 mg PO every day
Varicella-zoster virus	Significant exposure to varicella with no history of chickenpox or shingles, or no age-appropriate vaccination record	Vari ZIG 125 IU per 10 kg (max 625 IU) IM, <sup>†</sup> <b>OR</b> , if unavailable, IVIG 400 mg/kg $\times$ 1 dose administered $\leq$ 96 hr after exposure, ideally within 48 hr	If >96 hr from exposure, some experts recommend acyclovir 20 mg/kg (max 800 mg) PO four times daily for 5–7 days
<b>GENERALLY RECOMMENDED</b>			
<i>Toxoplasma gondii</i> <sup>*</sup>	IgG antibody to <i>Toxoplasma</i> and severe immunosuppression	TMP/SMX 150/750 mg/m <sup>2</sup> /day in two divided doses PO every day. Same alternative dosage schedules as for PCP prophylaxis	Dapsone (children $\geq$ 1 mo): 2 mg/kg or 15 mg/m <sup>2</sup> (maximum 25 mg) PO every day <b>PLUS</b> pyrimethamine 1 mg/kg (max 25 mg) PO every day <b>PLUS</b> leucovorin 5 mg PO daily every 3 days Atovaquone can also be used with or without pyrimethamine plus leucovorin
<b>NOT RECOMMENDED FOR MOST PATIENTS; INDICATED FOR USE ONLY IN UNUSUAL CIRCUMSTANCES</b>			
Cytomegalovirus (CMV)	CMV antibody positivity and severe immunosuppression (CD4 count < 50 cells/mm <sup>3</sup> )	Valganciclovir 900 mg PO once daily for older children who can receive adult dosing	None
Invasive bacterial infection	Hypogammaglobulinemia (IgG <400 mg/dL)	IVIG 400 mg/kg once every 2–4 weeks	None

<sup>\*</sup>Protection against *Toxoplasma* is provided by the preferred anti-*Pneumocystis* regimens. Pyrimethamine alone probably provides little if any protection.

<sup>†</sup>VariZIG may be obtained 24 hours a day from FFF Enterprises at 1-800-843-7477 or online at [www.fffenterprises.com](http://www.fffenterprises.com).

HIV, Human immunodeficiency virus; Ig, immunoglobulin; IVIG, intravenous immunoglobulin; PCP, *Pneumocystis jirovecii* (formerly *Pneumocystis carinii*) pneumonia; TMP/SMX, trimethoprim-sulfamethoxazole; VariZIG, human varicella immune globulin.

From Centers for Disease Control and Prevention. Guidelines for prevention and treatment of opportunistic infections in HIV exposed and HIV infected children. *MMWR Recomm Rep*. 2009;58(RR-11):127.

- (5) ART initiation should be considered in asymptomatic patients >12 months of age with plasma HIV RNA levels >100,000 copies/mL and in all patients who develop symptoms.
- b. Revised pediatric HIV classification system.
- c. Antiretroviral regimen: If an infant is identified as HIV infected while receiving ZDV prophylaxis, therapy should be changed to a three-drug regimen. For drug choices, refer to <http://www.aidsinfo.nih.gov/>.
- d. Clinical and laboratory monitoring in HIV-infected children: Immune status (CD4 count or percentage), viral load, and evidence of HIV progression (plasma HIV RNA) should be monitored at diagnosis and every 3–4 months. Other testing to perform at diagnosis includes HIV genotype, CBC with differential, serum chemistry with liver and renal function, lipid profile, and urinalysis. Drug toxicity should also be monitored on a regular basis. Careful attention to routine aspects of pediatric care (e.g., growth, development, vaccines) is essential. Screening for hepatitis B and C infection, as well as for tuberculosis, is also recommended for all HIV-infected patients.<sup>17</sup>
- e. Immunizations in HIV-infected or HIV-exposed infants and children: Perinatally exposed infants should receive all scheduled infant immunizations. Live vaccines, measles/mumps/rubella (MMR) and varicella vaccine should be given to asymptomatic HIV-infected children and adolescents (see Chapter 16). HIV-infected children should receive pneumococcal conjugated vaccine 23 (PCV23) at age 2 and 5 years. Influenza vaccine should be given annually in the fall to all infected children ≥age 6 months and to children ≥age 6 months who have HIV-infected household contacts.

## F. Tuberculosis (TB)

### 1. Types of testing<sup>8</sup>:

- a. **IGRA** (immunologic-based testing with interferon gamma release assay): Measures interferon-gamma (IFN- $\gamma$ ) production from T lymphocytes in response to stimulation with antigens that are fairly specific to *Mycobacterium tuberculosis* complex. Similar sensitivity to tuberculin skin test (TST) but higher specificity (because antigens used are not found in bacillus Calmette-Guérin (BCG) or most pathogenic nontuberculous mycobacteria):
  - (1) Testing of immune-competent children 5 years of age or older in place of a TST
  - (2) May be useful to determine whether a BCG-immunized child with a reactive TST more likely has latent TB infection or has a false-positive TST reaction caused by the BCG
- b. **TST**:
  - (1) Most common method for diagnosing latent TB infection in asymptomatic persons. BCG immunization is not a contraindication.
  - (2) Inject 5 tuberculin units (5 TU) of purified protein derivative (0.1 mL) intradermally with a 27-gauge needle on the volar aspect of the forearm to form a 6- to 10-mm wheal. Results of skin testing should be read 48–72 hours later.
  - (3) Definition of positive Mantoux test (regardless of whether BCG has been previously administered): [Box 17-1](#).

## BOX 17-1

DEFINITIONS OF POSITIVE TUBERCULIN SKIN TESTING<sup>9</sup>**INDURATION  $\geq$  5 MM**

Children in close contact with known or suspected contagious cases of tuberculosis  
 Children suspected to have tuberculosis based on clinical or radiographic findings  
 Children on immunosuppressive therapy or with immunosuppressive conditions (including HIV infection)

**INDURATION  $\geq$  10 MM**

Children at increased risk for dissemination based on young age (<4 yr) or with other medical conditions (cancer, diabetes mellitus, chronic renal failure, or malnutrition)  
 Children with increased exposure: those born in or whose parents were born in endemic countries; those with travel to endemic countries; those exposed to HIV-infected adults, homeless persons, illicit drug users, nursing home residents, incarcerated or institutionalized persons, migrant farm workers

**INDURATION  $\geq$  15 MM**

Children  $\geq$ 4 yr without any risk factors

- c. The incubation period from TB infection to a positive TST or IGRA is approximately 2–10 weeks.
2. **Who to test:**
  - a. Contacts of people with confirmed or suspected infectious TB (contact investigation)
  - b. Children with clinical or radiographic findings of TB
  - c. Children immigrating from or with history of travel to TB-endemic areas, including international adoptees; children with close contacts from TB-endemic areas (if the child is well, TST should be delayed for up to 10 weeks after return)
  - d. Children who will be starting T-cell suppressive immunomodulatory therapy
  - e. Annual testing for HIV-Infected children starting at age 3–12 months (TST only; IGRA not recommended)
  - f. Incarcerated adolescents
3. **Drug therapy:**
  - a. Treatment of latent TB infection:
    - (1) Indications:
      - (a) Children with positive tuberculin tests but no evidence of clinical disease
      - (b) Recent contacts, especially HIV-infected children, of people with infectious TB, even if tuberculin test and clinical evidence are not indicative of disease
    - (2) **Recommendations** (see **Formulary** for specific doses and **Table EC 17-C**):
      - (a) Isoniazid-susceptible: 9 months isoniazid daily (if daily therapy not possible, alternative is DOT [directly observed therapy] twice weekly for 9 months)

TABLE EC 17-C

## RECOMMENDED TREATMENT REGIMENS FOR DRUG-SUSCEPTIBLE TUBERCULOSIS IN INFANTS, CHILDREN, AND ADOLESCENTS

Infection or Disease Category	Regimen	Remarks
<b>Latent tuberculosis infection</b> (positive skin test or IGRA, no disease)		
Isoniazid-susceptible	9 months of isoniazid Q24 hr	If daily therapy is not possible, directly observed therapy (DOT) twice weekly may be used for 9 months.
Isoniazid-resistant	6 months of rifampin Q24 hr	If daily therapy is not possible, DOT twice weekly may be used for 6 months.
Isoniazid/rifampin-resistant <sup>a</sup>	Consultation with a tuberculosis specialist	For management of neonates born to mothers with evidence of tuberculosis infection, see American Academy of Pediatrics 2012 <i>Red Book</i> .
<b>Pulmonary and extrapulmonary (except meningitis)</b>	2 months of isoniazid, rifampin, ethambutol and pyrazinamide Q24 hr, followed by 4 months of isoniazid and rifampin <sup>b</sup> by DOT <sup>c</sup> 9–12 months of isoniazid and rifampin for drug-susceptible <i>Mycobacterium bovis</i>	If possible drug resistance is a concern, another drug (ethambutol or an aminoglycoside) is added to the initial three-drug therapy until drug susceptibilities are determined. DOT is highly desirable. Health department should be contacted.
<b>Meningitis</b>	2 months of isoniazid, rifampin, pyrazinamide, and an aminoglycoside, ethambutol, or ethionamide Q24 hr, followed by 7–10 months of isoniazid and rifampin Q24 hr or twice weekly (9–12 months total) At least 12 months of therapy without pyrazinamide for drug-susceptible <i>M. bovis</i>	A fourth drug (e.g., aminoglycoside) is given with initial therapy until drug susceptibility is known.

<sup>a</sup>Duration of therapy is longer in HIV-infected persons, and additional drugs may be indicated.

<sup>b</sup>Medications should be administered daily for first 2 weeks–2 months, then can be administered 2–3 times weekly by DOT.

<sup>c</sup>If initial chest x-ray shows cavitary lesions, and sputum after 2 months of therapy remains positive, duration of therapy is extended to 9 months.

Modified from American Academy of Pediatrics, Pickering LK, Baker CJ, Kimberlin DW, et al, eds. *Red Book: 2012 Report of the Committee on Infectious Diseases*. 28th ed. Elk Grove Village, Ill: AAP, 2012.



- (b) Isoniazid-resistant: 6 months of rifampin daily (alternative is DOT twice weekly for 6 months)
- (c) If resistant to isoniazid and rifampin, consult infectious disease specialist
- b. Treatment for active TB infection<sup>8</sup>: consultation with infectious disease specialist recommended. See Table EC 17-C. (For details, see 2012 American Academy of Pediatrics *Red Book*.)

## G. Selected Tickborne Illnesses<sup>9</sup>

For all of the following illnesses, infection typically occurs between spring and fall seasons.

1. **Lyme disease:**
  - a. Geographic distribution: New England and Middle Atlantic, Upper Midwest, and Pacific Northwest.
  - b. Presentation:
    - (1) *Early localized disease*: 3–32 days after tick bite. Erythema migrans (annular rash at site of bite, target lesion with clear or necrotic center), fever, headache, myalgia, malaise
    - (2) *Early disseminated disease*: 3–10 weeks after the tick bite. Secondary erythema migrans with multiple smaller target lesions, cranio-neuropathy (especially facial nerve palsy), systemic symptoms as previously listed, and lymphadenopathy; 1% may develop carditis with heart block or aseptic meningitis
    - (3) *Late disease*: Intermittent recurrent symptoms occur 2–12 months from initial tick bite. Pauciarticular arthritis affecting large joints (7% of those untreated), peripheral neuropathy, encephalopathy
  - c. Transmission: Spirochete *Borrelia burgdorferi*. Inoculation occurs by the bite of a deer tick, *Ixodes scapularis* or *Ixodes pacificus*; disseminates systemically through blood and lymphatics. Transmission of *B. burgdorferi* requires 24–48 hours of tick attachment.
  - d. Diagnosis:
    - (1) Early disease, clinical diagnosis: During first 4 weeks of infection, diagnostic tests are insensitive and generally not recommended.
    - (2) Early disseminated and late disease: Combination of clinical findings and serologic tests. A stepwise approach should be taken:
      - (a) First, perform a quantitative test for serum antibodies using EIA (enzyme immunoassay) or IFA (immunofluorescent assay). IgM will become detectable at 3–4 weeks and peak at 6–8 weeks. IgG is only used to confirm late diagnosis. Of note, false-positive results of these assays occur as result of cross-reactivity with viral infections, other spirochetal infections, and autoimmune diseases.
      - (b) If immunoassay is positive, Western blot should be used to confirm diagnosis. (If immunoassay is negative, no further testing indicated.)
      - (c) Lumbar puncture as clinically indicated. Lyme-disease-specific antibodies can be isolated from the cerebrospinal fluid (CSF) in patients with CNS involvement.

- e. Treatment: Antibiotic prophylaxis not routinely recommended for ticks attached <24–48 hours.
- (1) Early localized disease: Doxycycline 4 mg/kg (max 100 mg/dose) PO BID for 14–21 days is treatment of choice for patients  $\geq 8$  years. Amoxicillin or cefuroxime for 14–21 days recommended for younger children.
  - (2) Early disseminated and late-onset disease manifestations are treated by the same oral regimen as early disease, with the following durations: Multiple erythema migrans (21 days), isolated facial palsy (14–21 days), and arthritis (28 days). Persistent or recurrent arthritis (>2 months), carditis, meningitis, or encephalitis may be treated with ceftriaxone or parenteral penicillin (14–28 days).
2. **Rocky Mountain spotted fever<sup>8</sup>:**
- a. Geographic distribution: Widespread. Most common in south Atlantic, southeastern, and south central United States.
  - b. Presentation: Incubation period is  $\approx 1$  week (range 2–14 days):
    - (1) Symptoms: Fever, headache, myalgia, nausea, anorexia, abdominal pain, diarrhea. Severe disease may manifest in CNS, cardiac, pulmonary, gastrointestinal tract, renal involvement, disseminated intravascular involvement, and shock leading to death.
    - (2) Rash: Usually appears by day 6; initially erythematous and macular; progresses to maculopapular and petechial due to vasculitis. Rash usually appears on wrists and ankles and spreads proximally. Palms and soles are often involved.
    - (3) Laboratory manifestations: Thrombocytopenia, hyponatremia, and anemia. White blood cell count usually normal.
  - c. Transmission: *Rickettsia rickettsii*, an obligate intracellular pathogen transmitted to humans by a tick bite.
  - d. Diagnosis: By rickettsial group-specific serologic tests, which may be negative early in the illness. A fourfold or greater change between acute- and convalescent-phase serum specimens is diagnostic. Probable diagnosis can be established by a single serum titer of 1:64 or greater by IFA assay. Culture of *R. rickettsii* is generally not attempted because of danger of transmission to laboratory personnel. *R. rickettsii* can be obtained by immunohistochemical staining of tissue specimens obtained before initiation of antimicrobial therapy. This method is highly specific but not sensitive.
  - e. Treatment: Doxycycline is recommended drug for children of any age and should be started as soon as the diagnosis is suspected. Duration: 7–10 days and is continued until patient is afebrile for  $\geq 3$  days and has demonstrated clinical improvement.
  - f. For discussion of other rickettsial spotted fever infections that are clinically similar but epidemiologically distinct, see 2012 *Red Book* (Section 3).
3. **Ehrlichiosis<sup>8</sup>:**
- a. Geographic distribution: Southeastern, south central, and midwestern United States.

- b. Presentation: Systemic febrile illness with headache, chills, rigors, malaise, myalgia, arthralgia, nausea, vomiting, anorexia, or acute weight loss. Rash is variable in location and appearance:
  - (1) Laboratory manifestations: Leukopenia, anemia, and transaminitis are common. CSF studies with lymphocytic pleocytosis or elevated protein are also common.
  - (2) More severe disease: Pulmonary infiltrates, bone marrow hypoplasia, respiratory failure, encephalopathy, meningitis, disseminated intravascular coagulation (DIC), spontaneous hemorrhage, and renal failure.
- c. Transmission: *Ehrlichia chaffeensis* (human monocytic ehrlichiosis [HME]) and *Ehrlichia ewingii* associated with the bite of a Lone Star tick (*Amblyomma americanum*), although other tick species may be vectors. Mammalian reservoirs include white-tailed deer and white-footed mice.
- d. Diagnosis: Confirmed by isolation of *Ehrlichia* organisms from blood or CSF, a fourfold or greater change in IgG-specific antibody titer by IFA assay between acute and convalescent serum specimens, PCR assay amplification of ehrlichial DNA from a clinical specimen, or detection of an intraleukocytoplasmic cluster of bacteria in conjunction with a single IFA titer  $\geq 64$ . PCR from acute-phase peripheral blood of patients with ehrlichiosis seems sensitive, specific, and promising for early diagnosis.
- e. Treatment: Doxycycline 4 mg/kg/day BID IV or PO (max 100 mg/dose). Ehrlichiosis may be severe or fatal in untreated patients; initiate treatment early. Failure to respond within first 3 days should suggest infection with an agent other than *Ehrlichia*. Treatment should be continued for at least 3 days after defervescence, for a minimum total course of 7 days.
- 4. **Anaplasmosis:** Though clinically very similar, ehrlichiosis and anaplasmosis are now described separately. The previous information on clinical presentation and treatment is the same for anaplasmosis. Differences from ehrlichiosis are as follows: caused by *Anaplasma phagocytophilum* (human granulocytotropic anaplasmosis [HGA]), transmitted by the deer tick (*Ixodes scapularis*) or western black-legged tick (*Ixodes pacificus*), diagnosis via *Anaplasma* organisms using techniques as described previously. Most cases are reported from the north central and northeastern United States, and from northern California.

## H. Fungal and Yeast Infections

- 1. **Diagnosis:**
  - a. Place specimen (nail or skin scrapings, biopsy specimens, fluids from tissues or lesions) in 10% potassium hydroxide (KOH) on glass slide to look for hyphae, pseudohyphae.
  - b. Germ tube screen of yeast (3 hours) for *Candida albicans*: All germ tube–positive yeast are *C. albicans*, but not all *C. albicans* are germ tube positive.
- 2. **Common community-acquired fungal infections, etiology, and treatment** (Table 17-13)

TABLE 17-13

## COMMON COMMUNITY-ACQUIRED FUNGAL INFECTIONS

Disease	Usual Etiology	Suggested Therapy	Suggested Length of Therapy
Tinea capitis (ring-worm of scalp)	<i>Trichophyton tonsurans</i> , <i>Microsporum canis</i>	Oral griseofulvin (ultramicro): give with fatty foods. Fungal shedding decreased with 1%–2.5% selenium sulfide shampoo <i>Alt: terbinafine, itraconazole (total 2–4 weeks), or fluconazole (once weekly)</i>	4–8 wk or 2 wk after clinical resolution
Tinea corporis/pedis/cruris (ringworm of body/feet/genital region)	<i>Epidermophyton floccosum</i> , <i>Trichophyton rubrum</i> , <i>Trichophyton mentagrophytes</i> , <i>Microsporum canis</i>	Topical antifungal (miconazole, clotrimazole) once daily or BID; terbinafine BID	1–4 wks for either therapy
Oral candidiasis (thrush) in immunocompetent patients	<i>Candida albicans</i> , <i>Candida tropicalis</i>	Nystatin suspension or clotrimazole troche (only nystatin for infants)	7–10 days, then continue 3 days after clinical resolution
Candidal skin infections (intertriginous)	<i>C. albicans</i>	Topical nystatin, miconazole, clotrimazole	3 days after clinical resolution
Tinea unguium (ringworm of nails)	<i>T. mentagrophytes</i> , <i>T. rubrum</i> , <i>E. floccosum</i>	Oral griseofulvin <i>Alt: oral terbinafine, itraconazole, fluconazole</i>	6–12 mo 4–6 mo for alternatives (once weekly for fluconazole)

Modified from McMillan JA, Lee CKK, Siberry G, Dick J. *The Harriet Lane Handbook of Pediatric Antimicrobial Therapy*. Philadelphia: Mosby, 2009. See Table 1-5 for further details regarding treatment of fungal infections.

## I. Exposures to Bloodborne Pathogens and Postexposure Prophylaxis (PEP)

1. **HIV<sup>8,18,19</sup>**: Updated guidelines may be found at [aidsinfo.nih.gov](http://aidsinfo.nih.gov):
  - a. Occupational exposure, risk for occupational transmission of HIV:
    - (1) Needlesticks: Three infections for every 1000 exposures (0.3%). Risk is greater when exposure involves a larger volume of blood and/or higher titer of HIV, as in a deep injury, visible blood on the device causing the injury, a device previously used in the source patient's vein or artery, or a source patient in the late stages of HIV infection.
    - (2) Mucous membrane exposure: One infection for every 1000 exposures (0.1%). Risk may be higher with larger volume of blood and a higher titer of HIV, prolonged skin contact, extensive surface area of exposure, or skin integrity that is visibly compromised.
  - b. Nonoccupational HIV exposure in children and adolescents<sup>19</sup>:
    - (1) Injury from needles of discarded syringes: No confirmed reports of HIV acquisition from percutaneous injury by a needle found in the

community. If needle or syringe is found to have visible blood and source is known to be HIV infected, PEP should be considered.

Testing the syringe for HIV is not practical or reliable.

- (2) Repeated sexual encounters or a single episode of sexual abuse: Risk is highest with unprotected receptive anal intercourse (5 per 1,000 exposures), intermediate with receptive vaginal intercourse (1 per 1,000 exposures), and even lower with insertive vaginal intercourse. If exposure source has genital ulcer disease or another sexually transmitted infection, or if there was tissue damage, risk for HIV transmission is higher, increasing the benefit of PEP relative to burden and risk for drug toxicity.
- (3) Human milk<sup>14</sup>: PEP is not warranted for a single exposure to human breast milk.
- (4) Human bites: Transmission is extremely rare even when saliva is contaminated with blood. Saliva inhibits HIV infectivity; HIV is rarely isolated from saliva, and concentrations of HIV in saliva of HIV-infected persons is low even in the presence of periodontal disease.

c. Prophylaxis:

- (1) Optimally, PEP should be initiated as soon as possible, preferably within 1–3 hours of exposure but no later than 72 hours. The usual duration of PEP, if tolerated, is 28 days. The benefits of PEP are greatest when risk of infection is high, intervention is prompt, and adherence is likely.
- (2) A clinician with experience in treating individuals with HIV infection should be consulted whenever possible (without causing PEP initiation delay) before initiating therapy. Decision about need for PEP is based on HIV status of source, type and severity of potential exposure, and individual risk tolerance. PEP generally comprises two-drug or three-drug regimens, frequently available in fixed-dose combination pills for older children and adults. No clear evidence of superior efficacy of a three-drug regimen over a two-drug regimen in preventing HIV infection after exposure, but many experts prefer to use three drugs; this practice must be balanced against the increased toxicity potential when additional drugs are used. Typical regimens include two nucleoside reverse-transcriptase inhibitors (NRTIs) (e.g., ZDV + lamivudine or, in adolescent/adults, tenofovir + emtricitabine), two NRTIs plus a protease inhibitor (PI) (e.g., lopinavir/ritonavir) or two NRTIs plus a non-nucleoside reverse-transcriptase inhibitor (NNRTI) (e.g., efavirenz). Full descriptions of potential regimens can be found in CDC and American Academy of Pediatrics (AAP) guidelines.
- (3) Use of ZDV alone as PEP is no longer recommended. For most recent recommendations, refer to CDC and AAP guidelines. The CDC's PEP hotline (open 24 hours daily) is 888-448-4911.

2. **Hepatitis B:** Most readily transmitted of the bloodborne pathogens.

Recommendations for hepatitis B prophylaxis in nonimmune person after percutaneous exposure to blood that contains (or might contain)

hepatitis B surface antigen (HBsAg) include hepatitis B immune globulin and initiation of hepatitis B vaccine series. For details, see Chapter 16.

3. **Hepatitis C:** No preventive therapy available. Serologic testing and follow-up are important to document if infection occurs. Infections become chronic in the majority of patients.

#### J. Infectious Diseases in Internationally Adopted Children

For more information, see American Academy of Pediatrics. Medical evaluation of internationally adopted children for infectious diseases. In: Pickering LK, Baker CJ, Kimberlin DW, et al, eds. *Red Book: 2012 Report of the Committee on Infectious Diseases*. 29th ed. Elk Grove Village, Ill: AAP, 2012.<sup>8</sup>

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# Chapter 18

## Neonatology

Lauren Beard, MD

 See additional content on Expert Consult

### I. WEBSITES

[www.nicuniversity.org](http://www.nicuniversity.org)

Outcomes calculator: [http://www.nichd.nih.gov/about/org/der/branches/ppb/programs/epbo/pages/epbo\\_case.aspx](http://www.nichd.nih.gov/about/org/der/branches/ppb/programs/epbo/pages/epbo_case.aspx)

Neonatal dermatology: <http://www.adhb.govt.nz/newborn/TeachingResources/Dermatology/Dermatology.htm>

### III. NEWBORN RESUSCITATION

#### A. Neonatal Advanced Life Support (NALS) Algorithm for Neonatal Resuscitation (Fig. 18-1)

For infants with meconium in the amniotic fluid, routine intrapartum oropharyngeal and nasopharyngeal **suctioning is not recommended**.

If the infant is not vigorous, endotracheal intubation should be performed immediately after birth, and suction should be applied to the endotracheal tube as it is withdrawn.<sup>1</sup>

#### B. Endotracheal Tube Size and Depth of Insertion (see Table 18-1)

#### C. Ventilatory Support (See Chapter 4)

#### D. Vascular Access (See Chapter 3 for Umbilical Venous Catheter and Umbilical Artery Catheter Placement)

**NOTE:** During initial resuscitation, umbilical venous catheter (UVC) should be inserted just far enough to obtain blood return; no measurement or verified placement necessary initially.

### IV. NEWBORN ASSESSMENT

#### A. Vital Signs and Birth Weight

1. **Normal vital signs:** HR 120–160 bpm, respiratory rate (RR) 40–60 breaths/min, rectal temperature 36.5°–37.5°C
2. **Arterial blood pressure:** Related to birth weight, gestational age (see Chapter 7).
3. **See Chapter 21 for growth charts for the premature infant.**
4. **Weight:** Extremely low birth weight (ELBW) < 1000 g, very low birth weight (VLBW) < 1500 g, low birth weight (LBW) < 2500 g, small for gestational age (SGA) < 10% for gestational age, large for gestational age (LGA) > 90% for gestational age

#### B. Apgar Scores (Table 18-2)

Assess at 1 and 5 minutes. Repeat at 5-minute intervals if 5-minute score is <7.<sup>2</sup>



## II. FETAL ASSESSMENT

### A. Fetal Anomaly Screening

#### 1. Fetal karyotyping:

- Chorionic villus sampling: Segment of placenta obtained either transcervically or transabdominally at 8–11 weeks' gestation. Detects chromosomal abnormalities and metabolic disorders but cannot detect neural tube defects or measure  $\alpha$ -fetoprotein (AFP). Complications include pregnancy loss (0.5%–2%), maternal infection, increased risk for fetomaternal hemorrhage, and fetal limb and jaw malformation.
- Amniocentesis: 20–30 mL of amniotic fluid is withdrawn under ultrasound guidance after 16–18 weeks' gestation. Detects chromosomal abnormalities, metabolic disorders, and neural tube defects. Complications include pregnancy loss (<5/1000), chorioamnionitis (<1/1000), leakage of amniotic fluid (1/300), and fetal scarring or dimpling of the skin.

#### 2. Routine ultrasound: Performed at 18–20 weeks' gestation

#### 3. Maternal AFP (Box EC 18-A)

#### 4. Amniotic fluid volume estimation and amniotic fluid index (AFI) (Box EC 18-B). AFI calculated with ultrasound by adding together width of amniotic fluid pockets in four quadrants

#### 5. Biophysical profile test (Table EC 18-A)

### B. Estimation of Gestational Age

- Last menstrual period (LMP).** Nägele rule gives most accurate determination of gestational age:

$$\text{Estimated due date} = (\text{LMP} - 3 \text{ months}) + 7 \text{ days}$$

- Ultrasound:** Crown-rump length obtained between 6 and 12 weeks' gestation predicts gestational age  $\pm$  3–4 days. After 12 weeks, the biparietal diameter is accurate within 10 days; beyond 26 weeks, accuracy diminishes to  $\pm$  3 weeks.
- Postmenstrual age:** Gestational age + chronologic age in weeks. Used in perinatal period during hospitalization and until 2 years of age.

#### BOX EC 18-A

##### MATERNAL $\alpha$ -FETOPROTEIN ASSOCIATIONS

###### Elevated (>2.5 multiples of the median)

Incorrect gestational dating  
Neural tube defects  
Anencephaly  
Multiple pregnancy  
Turner syndrome  
Omphalocele  
Cystic hygroma  
Epidermolysis bullosa  
Renal agenesis

###### Low (<0.75 multiples of the median)

Underestimation of gestational age  
Intrauterine growth retardation  
Trisomy 13  
Trisomy 18  
Down syndrome

BOX EC 18-B	
AMNIOTIC FLUID VOLUME ESTIMATION AND AMNIOTIC FLUID INDEX (AFI)	
Oligohydramnios (<500 mL)/(AFI 0–5)	Polyhydramnios (>2L)/(AFI >25)
Renal and urologic anomalies: Potter syndrome Lung hypoplasia Limb deformities Premature rupture of membranes Placental insufficiency	GI anomalies: gastroschisis, duodenal atresia, tracheoesophageal fistula, diaphragmatic hernia, esophageal atresia ± tracheoesophageal atresia CNS anomalies associated with impaired swallowing: anencephaly, Werdnig-Hoffman syndrome, spinomuscular atrophy (SMA) Chromosomal trisomies Maternal diabetes Cystic adenomatoid malformation of the lung

CNS, Central nervous system; GI, gastrointestinal.

TABLE EC 18-A		
THE BIOPHYSICAL PROFILE		
Biophysical Variable	Normal (Score = 2)	Abnormal (Score = 0)
Fetal breathing movements	1 or more episodes of ≥20 sec within 30 min	Absent or no episode of ≥20 sec within 30 min
Gross body movements	2 or more discrete body/limb movements within 30 min (episodes of active continuous movement considered as a single movement)	<2 episodes of body/limb movements within 30 min
Fetal tone	1 or more episodes of active extension with return to flexion of fetal limb(s) or trunk (opening and closing of hand considered normal tone)	Slow extension with return to partial flexion, movement of limb in full extension, absent fetal movement, or partially open fetal hand
Reactive fetal heart rate	2 or more episodes of acceleration of ≥15 bpm* and >15 sec within 20 min, associated with fetal movement	1 or more episodes of acceleration of fetal heart rate or acceleration of <15 bpm within 20 min
Qualitative amniotic fluid volume	1 or more pockets of fluid measuring ≥2 cm in vertical axis	Either no pockets or largest pocket <2 cm in vertical axis

\*bpm, Beats per minute.  
 Modified from Manning FA. Fetal biophysical profile. Obstet Gynecol Clin North Am. 26(4):557-577, 1999.

**C. Expected Birth Weight by Gestational Age (Table 18-1)**

**D. Intrapartum Fetal Heart Rate (FHR) Monitoring**

- Normal baseline FHR:** 120–160 beats/min (bpm). Mild bradycardia is 100–120 bpm. Severe bradycardia is <90 bpm.
- Normal beat-to-beat variability:** Deviation from baseline of >6 bpm. Absence of variability is <2 bpm from baseline and is a sign of potential fetal distress, particularly when combined with variable or late decelerations.

3. **Accelerations:** Associated with fetal movement, are benign, and indicate fetal well-being
4. **Decelerations:**
  - a. Early decelerations: Begin with onset of contractions. Heart rate reaches nadir at peak of contraction and returns to baseline as contraction ends. Occur secondary to changes in vagal tone after brief hypoxic episodes or head compression and are benign.
  - b. Variable decelerations: Represent umbilical cord compression and have no uniform temporal relationship to onset of contraction. Considered severe when heart rate drops to <60 bpm for about 60 seconds, with slow recovery to baseline.
  - c. Late decelerations: Occur after peak of contraction, persist after contraction stops, and show a slow return to baseline. Result from uteroplacental insufficiency and indicate fetal distress.

TABLE 18-1

**PREDICTED ENDOTRACHEAL TUBE SIZE AND DEPTH BY BIRTH WEIGHT AND GESTATIONAL AGE**

Gestational Age (wk)	Weight (g)	ETT Size (mm)	ETT Depth of Insertion (cm from Upper Lip)
23–24	500–600	2.5	5.5
25–26	700–800	2.5	6
27–29	900–1000	2.5	6.5
30–32	1100–1400	2.5–3.0	7
33–34	1500–1800	3.0	7.5
35–37	1900–2400	3.0–3.5	8
38–40	2500–3100	3.5	8.5

**NOTE:** Based on Tochen's 1979 study, the "7-8-9-10" rule recommended that 1-, 2-, 3-, or 4-kg babies were to be intubated at a "tip to lip" distance of 7, 8, 9, or 10 cm, respectively. However, recent literature suggests these guidelines may better represent appropriate endotracheal tube (ETT) depth of insertion.

Data from Peterson J, Johnson N, Deakins K, et al. Accuracy of the 7-8-9 rule for endotracheal tube placement in the neonate. *J Perinatol.* 2006;26:333–336.

### C. New Ballard Gestational Age Estimation

The Ballard score is most accurate when performed between age 12 and 20 hours.<sup>3</sup> Approximate gestational age is calculated based on the sum of the neuromuscular and physical maturity ratings (Fig. 18-2).

#### 1. Neuromuscular maturity:

- Posture: Observe infant quiet and supine. Score 0 for arms, legs extended; 1 for starting to flex hips and knees, arms extended; 2 for stronger flexion of legs, arms extended; 3 for arms slightly flexed, legs flexed and abducted; and 4 for full flexion of arms and legs.
- Square window: Flex hand on forearm enough to obtain fullest possible flexion without wrist rotation. Measure angle between hypothenar eminence and ventral aspect of forearm.
- Arm recoil: With infant supine, flex forearms for 5 seconds, fully extend by pulling on hands, then release. Measure the angle of elbow flexion to which arms recoil.
- Popliteal angle: Hold infant supine with pelvis flat, thigh held in knee-chest position. Extend leg by gentle pressure and measure popliteal angle.
- Scarf sign: With baby supine, pull infant's hand across the neck toward opposite shoulder. Determine how far elbow will reach across. Score 0 if elbow reaches opposite axillary line, 1 if past midaxillary line, 2 if past midline, and 3 if elbow unable to reach midline.
- Heel-to-ear maneuver: With baby supine, draw foot as near to head as possible without forcing it. Observe distance between foot and head and degree of extension at knee.

2. **Physical maturity:** Based on developmental stage of eyes, ears, breasts, genitalia, skin, lanugo, and plantar creases (see Fig. 18-2)

### D. Birth Trauma

- Extradural fluid collections** (Table 18-3, Fig. 18-3):

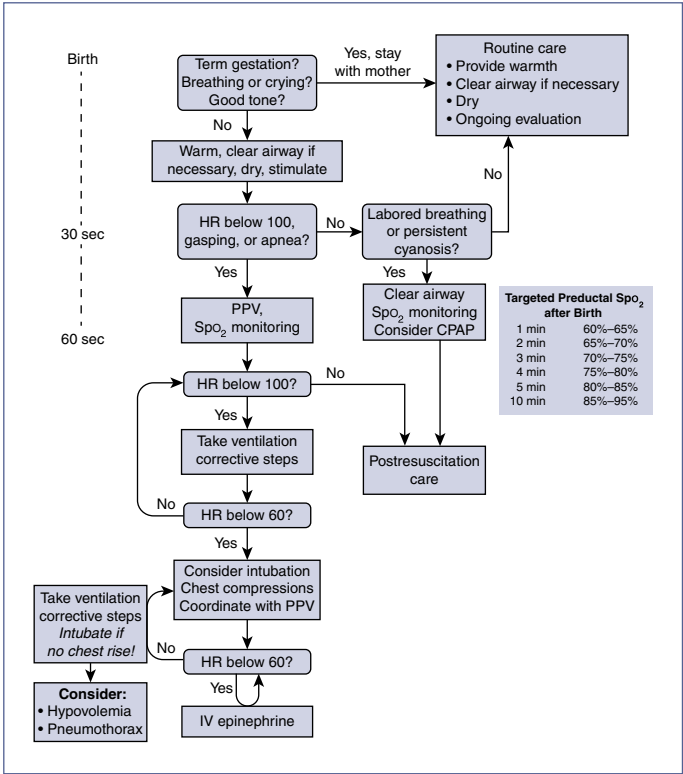


FIGURE 18-1

Overview of resuscitation in the delivery room. CPAP, Continuous positive airway pressure; HR, heart rate; IV, intravenous; PPV, positive pressure ventilations; SpO<sub>2</sub>, oxygen saturation by pulse oximetry. (From Kattwinkel J, Perlman JM, Aziz K, et al. 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Part 15: Neonatal resuscitation. Circulation. 2010;122:S909–S919.)

TABLE 18-2

APGAR SCORES

Score	0	1	2
Heart rate	Absent	<100 bpm	>100 bpm
Respiratory effort	Absent, irregular	Slow, crying	Good
Muscle tone	Limp	Some flexion of extremities	Active motion
Reflex irritability (nose suction)	No response	Grimace	Cough or sneeze
Color	Blue, pale	Acrocyanosis	Completely pink

Data from Apgar V. Proposal for a new method of evaluation of the newborn infant. *Anesth Analg*. 1953;32:260.

# Neuromuscular maturity

Neuromuscular maturity sign	Score							Record score here
	-1	0	1	2	3	4	5	
Posture								
Square window (wrist)	 > 90°	 90°	 60°	 45°	 30°	 0°		
Arm recoil		 180°	 140-180°	 110-140°	 90-110°	 < 90°		
Popliteal angle	 180°	 160°	 140°	 120°	 100°	 90°	 < 90°	
Scarf sign								
Heel to ear								
TOTAL NEUROMUSCULAR MATURITY SCORE								

# Physical maturity

Physical maturity sign	Score							Record score here
	-1	0	1	2	3	4	5	
Skin	Sticky, friable, transparent	Gelatinous, red, translucent	Smooth, pink, visible veins	Superficial peeling and/or rash, few veins	Cracking, pale areas, rare veins	Parchment, deep cracking, no vessels	Leathery, cracked, wrinkled	
Lanugo	None	Sparse	Abundant	Thinning	Bald areas	Mostly bald		
Plantar surface	Heel-toe: 40-50 mm: -1 <40 mm: -2	>50 mm, no crease	Faint red marks	Anterior transverse crease only	Creases anterior two thirds	Creases over entire sole		
Breast	Imperceptible	Barely perceptible	Flat areola, no bud	Stippled areola, 1-2 mm bud	Raised areola, 3-4 mm bud	Full areola, 5-10 mm bud		
Eye/ear	Lids fused: loosely: -1 tightly: -2	Lids open, pinna flat, stays folded	Sl. curved pinna, soft, slow recoil	Well-curved pinna, soft but ready recoil	Formed and firm, instant recoil	Thick cartilage, ear stiff		
Genitals (male)	Scrotum flat, smooth	Scrotum empty, faint rugae	Testes in upper canal, rare rugae	Testes descending, few rugae	Testes down, good rugae	Testes pendulous, deep rugae		
Genitals (female)	Clitoris prominent and labia flat	Prominent clitoris and small labia minora	Prominent clitoris and enlarging minora	Majora and minora equally prominent	Majora large, minora small	Majora cover clitoris and minora		
TOTAL PHYSICAL MATURITY SCORE								

Score	Maturity rating																	Gestational age (weeks)	
Neuromuscular	Score	-10	-5	0	5	10	15	20	25	30	35	40	45	50	By dates				_____
Physical															By ultrasound				_____
Total	Weeks	20	22	24	26	28	30	32	34	36	38	40	42	44	By exam				_____

**FIGURE 18-2**

Neuromuscular and physical maturity (New Ballard Score). (Modified from Ballard JL et al. New Ballard Score, expanded to include extremely premature infants. J Pediatr. 1991;119:417-423.)

- 2. **Fractured clavicle:** Possible crepitus/deformity on day 1 ± swelling/discomfort on day 2
- 3. **Brachialplexus injuries:** Erb palsy (C5-6) most common, but also possible to have Klumpke (C8-T1; least common) and total brachial plexus palsy (C5-T1). See [Section XII](#).

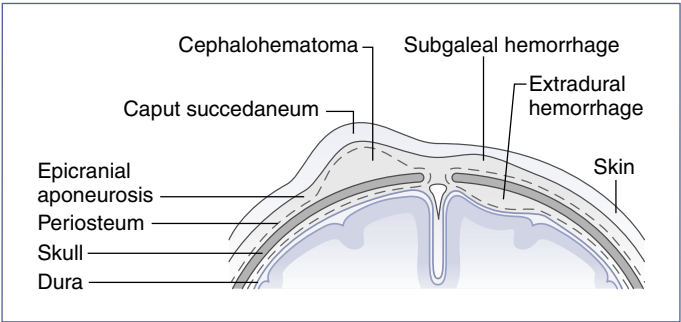
**E. Neonatal Hypoxic-Ischemic Encephalopathy (HIE): Initial Management<sup>4</sup>**

- 1. **Hypothermia protocol:** Infants with evidence of HIE shortly after birth who are > 36 weeks' gestation should be considered for hypothermia. Protocol should be initiated within 6 hours of delivery.
- 2. **Criteria for hypothermia vary by center but typically include one or more of the following:**
  - a. Cord gas or blood gas in the first hour of life with a pH <7.0 or base deficit of >16. For infants with a pH of 7.01–7.15 or base deficit of 10–15.9, additional criteria should be met (e.g., significant perinatal event).

**TABLE 18-3**  
**BIRTH-RELATED EXTRADURAL FLUID COLLECTIONS**

	Caput Succedaneum	Cephalohematoma	Subgaleal Hemorrhage
<b>Location</b>	At point of contact; can extend across sutures	Usually over parietal bones; does not cross sutures	Beneath epicranial aponeurosis; may extend to orbits or nape of neck
<b>Findings</b>	Vaguely demarcated; pitting edema, shifts with gravity	Distinct margins; initially firm, more fluctuant after 48 hr	Firm to fluctuant, ill-defined borders; may have crepitus or fluid waves
<b>Timing</b>	Maximal size/firmness at birth; resolves in 48–72 hrs	Increases after birth for 12–24 hr; resolution over weeks	Progressive after birth; resolution over weeks
<b>Size</b>	Minimal	Rarely severe	May be severe, especially in the setting of associated coagulopathy

Data from DJ Davis. Neonatal subgaleal hemorrhage: diagnosis and management. *CMAJ*. 2001;164:1452.



**FIGURE 18-3**  
Types of extradural fluid collections seen in newborn infants.

- b. 10-minute APGAR  $\leq 5$
- c. Evidence of moderate to severe encephalopathy
- d. Need for assisted ventilation at birth for at least 10 minutes

#### F. Selected Anomalies, Syndromes, and Malformations (See Chapter 13 for Common Syndromes/Genetic Disorders)

1. **VATER association:** Vertebral anomalies, Anal anomalies and anal atresia, Tracheoesophageal fistula, Esophageal atresia, and Radial and/or Renal defects. May also include vascular (cardiac) defects.
2. **CHARGE syndrome** (associated with mutations in gene *CHD7* on chromosome 8q12): Coloboma, Heart disease, choanal Atresia, Retarded growth and development (may include central nervous system [CNS] anomalies), Genital anomalies (may include hypogonadism), Ear abnormalities or deafness.
3. **Infant of a diabetic mother:** Sacral agenesis, femoral hypoplasia, heart defects, and cleft palate. May also include preaxial radial defects, microtia, cleft lip, microphthalmos, holoprosencephaly, microcephaly, anencephaly, spina bifida, hemivertebra, urinary tract defects, and polydactyly.
4. **Fetal alcohol syndrome:** SGA, short palpebral fissures, epicanthal folds, flat nasal bridge, long philtrum, thin upper lip, small hypoplastic nails. May be associated with cardiac defects.

### V. FLUIDS, ELECTROLYTES, AND NUTRITION

#### A. Fluids

1. **Insensible water loss in preterm infants (Table 18-4).**
2. **Water requirements of newborns (Table 18-5).**

#### B. Glucose

1. **Requirements:** Preterm neonates require about 5–6 mg/kg/min of glucose (40–100 mg/dL).<sup>5</sup> Term neonates require about 3–5 mg/kg/min of glucose. The formula to calculate glucose infusion rate (GIR) is as follows:

$$\begin{aligned} \text{GIR (mg/kg/min)} &= [(\% \text{ glucose in solution} \times 10 \times \\ &\quad \text{rate of infusion per hour}) / (60 \times \text{weight (kg)})] \\ &= 0.167 \times (\% \text{ glucose}) \times (\text{infusion rate}) / \text{weight (kg)} \end{aligned}$$

2. **Management of hyperglycemia and hypoglycemia (Table 18-6, Fig. 18-4).**<sup>6</sup> Also see Chapter 10.

#### C. Electrolytes, Minerals, and Vitamins

1. **Electrolyte requirements (Table 18-7)**
2. **Mineral and vitamin requirements:**
  - a. Infants born at <34 weeks' gestation have higher calcium, phosphorus, sodium, iron, and vitamin D requirements and require breast-milk fortifier or special preterm formulas with iron. Fortifier should be added to breast milk only after the second week of life.



TABLE 18-4

## INSENSIBLE WATER LOSS IN PRETERM INFANTS\*

Body Weight (g)	Insensible Water Loss (mL/kg/day)
<1000	60–70
1000–1250	60–65
1251–1500	30–45
1501–1750	15–30
1751–2000	15–20

\*Estimates of insensible water loss at different body weights during the first few days of life.

Data from Veille JC. Management of preterm premature rupture of membranes. *Clin Perinatol*. 1988;15:851-862.

TABLE 18-5

## WATER REQUIREMENTS OF NEWBORNS

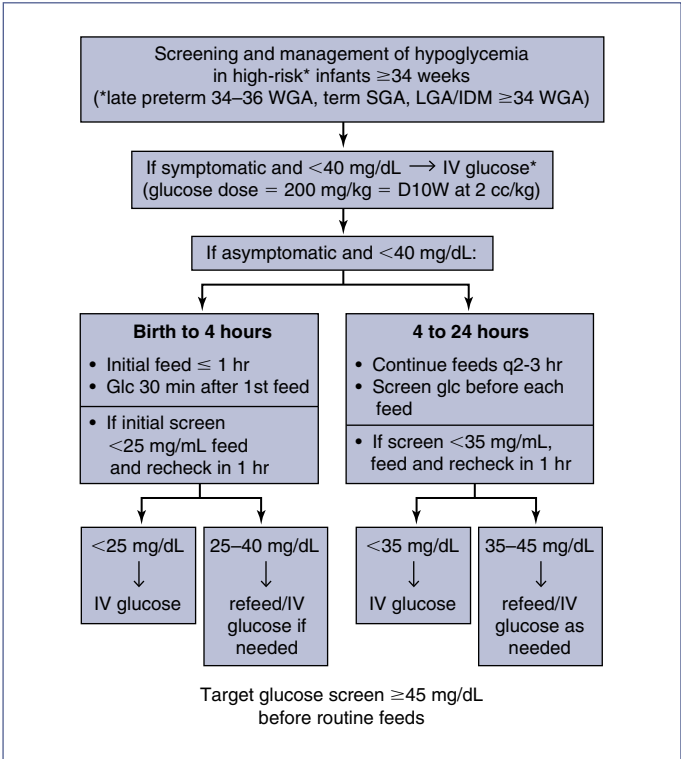
Birth Weight (g)	Water Requirements (mL/kg/24 hr) by Age		
	1–2 days	3–7 days	7–30 days
<750	100–250	150–300	120–180
750–1000	80–150	100–150	120–180
1000–1500	60–100	80–150	120–180
>1500	60–80	100–150	120–180

Data from Taeusch HW, Ballard RA, eds. *Schaeffer and Avery's Diseases of the Newborn*. 7th ed. Philadelphia: WB Saunders, 1998.

TABLE 18-6

MANAGEMENT OF HYPERGLYCEMIA AND HYPOGLYCEMIA<sup>6</sup>

	Hypoglycemia	Hyperglycemia
Definition	Serum glucose < 40 mg/dL in term and late preterm infants	Serum glucose > 125 mg/dL in term infants, >150 mg/dL in preterm infants
Differential diagnosis	Insufficient glucose delivery Decreased glycogen stores Increased circulating insulin (infant of a diabetic mother, maternal drugs, Beckwith-Wiedemann syndrome, tumors) Endocrine and metabolic disorders Sepsis or shock Hypothermia, polycythemia, or asphyxia	Excess glucose administration Sepsis Hypoxia Hyperosmolar formula Neonatal diabetes mellitus Medications
Evaluation	Assess for symptoms and calculate glucose delivery to infant. Laboratory evaluation: serum glucose (bedside); complete blood cell count with differential; electrolytes; blood, urine, $\pm$ cerebrospinal fluid (CSF) cultures; urinalysis; insulin and C-peptide levels if warranted.	
Management	(See Fig. 18-4.) If glucose < 40 and symptomatic, treat with intravenous glucose (dose = 200 mg/kg, which is equivalent to dextrose 10% at 2 mL/kg). Change dextrose infusion rates gradually. Generally, no more than 2 mg/kg/min in a 2-hr interval. (See Chapter 10 for further guidelines.) Monitor glucose levels every 30–60 min until normal.	Gradually decrease glucose infusion rate if receiving >5 mg/kg/min. Monitor glucosuria. Consider insulin infusion for persistent hyperglycemia.



**FIGURE 18-4**

Screening for and management of postnatal glucose homeostasis in late-preterm (34–36 6/7 weeks) and term small-for-gestational-age and large-for-gestational-age infants of diabetic mothers. D10W, 10% dextrose in water; glc, glucose; IDM, infant of diabetic mother; IV, intravenous; LGA, large for gestational age; SGA, small for gestational age; WGA, weeks gestational age. (Modified from Adamkin DH, Committee on Fetus and Newborn. Postnatal glucose homeostasis in late-preterm and term infants. Pediatrics. 2011;127:575–579).

**TABLE 18-7**

**ELECTROLYTE REQUIREMENTS**

	Before 48 Hours of Life	After 48–72 Hours of Life
Sodium	None unless serum sodium < 135 mEq/L, without evidence of volume overload	Term infants: 2–3 mEq/kg/day Preterm infants: 3–5 mEq/kg/day
Potassium	None	1–2.5 mEq/kg/day if adequate urine output is established and serum level < 4.5 mEq/L

- b. Iron: Enterally fed preterm infants require elemental iron supplementation of 2 mg/kg/day after age 4–8 weeks.

#### D. Nutrition

1. **Growth and caloric requirements:**
  - a. Preterm infants (healthy and thermoneutral environments):
    - (1) Caloric requirements: 115–130 kcal/kg/day (up to 150 kcal/kg/day for very low-birth-weight infants)
    - (2) Growth (after 10 days of life): 15–20 g/kg/day
  - b. Term infants:
    - (1) Caloric requirements: 100–120 kcal/kg/day
    - (2) Growth (after 10 days of life): 10 g/kg/day
2. **Total parenteral nutrition (see Chapter 21)**

### VI. CYANOSIS IN THE NEWBORN

#### A. Differential Diagnosis

1. **General:** Hypothermia, hypoglycemia, sepsis, shock
2. **Neurologic:** Central apnea, central hypoventilation, intraventricular hemorrhage (IVH), meningitis
3. **Respiratory:** Persistent pulmonary hypertension of the newborn (PPHN), diaphragmatic hernia, pulmonary hypoplasia, choanal atresia, pneumothorax, respiratory distress syndrome (RDS), transient tachypnea of the newborn (TTN), pneumonia, meconium aspiration
4. **Cardiac:** Congestive heart failure, congenital cyanotic heart disease
5. **Hematologic:** Polycythemia, methemoglobinemia
6. **Medications:** Respiratory depression from maternal medications (e.g., magnesium sulfate, narcotics)

#### B. Evaluation

1. **Physical examination:** Note central vs. peripheral and persistent vs. intermittent cyanosis, respiratory effort, single vs. split  $S_2$ , presence of heart murmur. Acrocyanosis is often a normal finding in newborns.
2. **Clinical tests:** Oxygen challenge test (see Chapter 7), preductal/postductal arterial blood gases or pulse oximetry to assess for right-to-left shunt, and transillumination of chest for possible pneumothorax.
3. **Other data:** Complete blood cell count (CBC) with differential, serum glucose, chest radiograph, electrocardiogram (ECG), echocardiography. Consider blood, urine, and cerebrospinal fluid (CSF) cultures if sepsis is suspected, and methemoglobin level if cyanosis is out of proportion to hypoxemia.

### VII. RESPIRATORY DISEASES

#### A. General Respiratory Considerations

1. **Exogenous surfactant therapy:**
  - a. Indications: RDS in preterm infants, meconium aspiration, pneumonia, persistent pulmonary hypertension.

- b. Administration: If infant is  $\leq 26$  weeks' gestation, first dose is typically given in delivery room or as soon as stabilized; repeat dosing may follow at 6-hour intervals.
- c. Complications: Pneumothorax, pulmonary hemorrhage.
- 2. **Supplemental O<sub>2</sub>:** Adjust inspired oxygen to maintain O<sub>2</sub> saturation between 85% and 94% until retina is fully vascularized, between 94% and 98% if retinas are mature (see [Section XIII](#)), and  $>97\%$  in cases of pulmonary hypertension.

## **B. Respiratory Distress Syndrome**

- 1. **Definition:** Deficiency of pulmonary surfactant (a phospholipid protein mixture that decreases surface tension and prevents alveolar collapse). Surfactant is produced by type II alveolar cells in increasing quantities from 32 weeks' gestation:
  - a. Maternal administration of steroids antenatally has been shown to decrease neonatal morbidity and mortality. Risk for RDS is decreased in babies born  $>24$  hours and  $<7$  days after maternal steroid administration.
  - b. Other factors that accelerate lung maturity: Maternal hypertension, sickle cell disease, narcotic addiction, intrauterine growth retardation, prolonged rupture of membranes, and fetal stress
- 2. **Incidence:**
  - a.  $<30$  weeks' gestation: 60% without antenatal steroids, 35% in those who received antenatal steroids
  - b. 30–34 weeks' gestation: 25% without antenatal steroids, 10% in those who received antenatal steroids
  - c.  $>34$  weeks' gestation: 5%
- 3. **Risk factors:** Prematurity, maternal diabetes, cesarean section without antecedent labor, perinatal asphyxia, second twin, previous infant with RDS.
- 4. **Clinical presentation:** Respiratory distress worsens during first few hours of life, progresses over 48–72 hours, and subsequently improves:
  - a. Recovery is accompanied by brisk diuresis.
  - b. Chest x-ray findings: *Reticulogranular* pattern to lung fields; may obscure heart borders.
- 5. **Management:**
  - a. Support ventilation and oxygenation
  - b. Surfactant therapy

## **C. Persistent Pulmonary Hypertension of the Newborn (PPHN)**

- 1. **Etiology:** Idiopathic or secondary to conditions leading to increased pulmonary vascular resistance. Most commonly seen in term or postterm infants, infants born by cesarean section, and infants with a history of fetal distress and low Apgar scores. Usually presents within 12–24 hours of birth:
  - a. Vasoconstriction secondary to hypoxemia and acidosis (e.g., neonatal sepsis)
  - b. Interstitial pulmonary disease (meconium aspiration syndrome, pneumonia)

- c. Hyperviscosity syndrome (polycythemia)
- d. Pulmonary hypoplasia, either primary or secondary to congenital diaphragmatic hernia or renal agenesis
- 2. **Diagnostic features:**
  - a. Severe hypoxemia ( $P_{aO_2} < 35\text{--}45$  mm Hg in 100%  $O_2$ ) disproportionate to radiologic changes
  - b. Structurally normal heart with right-to-left shunt at foramen ovale and/or ductus arteriosus; decreased postductal oxygenation compared with preductal (difference of at least 7–15 mm Hg between preductal and postductal  $P_{aO_2}$  is significant)
  - c. Must be distinguished from cyanotic heart disease. Infants with heart disease will have an abnormal cardiac examination and show little to no improvement in oxygenation with increased fraction of inspired  $O_2$  ( $F_{IO_2}$ ) and hyperventilation. See Chapter 7 for interpretation of oxygen challenge test.
- 3. **Principles of therapy:**
  - a. **Improve oxygenation:** Supplemental oxygen ( $F_{IO_2}$ ) to improve alveolar oxygenation. Optimize oxygen-carrying capacity with blood transfusions as needed.
  - b. **Minimize pulmonary vasoconstriction:**
    - (1) Minimal handling of infant and limited invasive procedures. Sedation and occasionally paralysis of intubated neonates may be necessary.
    - (2) Alkalosis (pH 7.45–7.55): Metabolic or respiratory ( $P_{CO_2}$  in low 30s); may improve oxygenation, although not noted to affect outcome. Avoid severe hypocarbia ( $P_{CO_2} < 30$ ), which can be associated with myocardial ischemia and decreased cerebral blood flow. Hyperventilation may result in barotrauma, predisposing to chronic lung disease, so should be minimized if possible. Consider high-frequency ventilation.
  - c. **Maintenance of systemic blood pressure and perfusion:** Reversal of right-to-left shunt through volume expanders and/or inotropes.
  - d. **Consider pulmonary vasodilator therapy:**
    - (1) Inhaled nitric oxide (NO): Reduces pulmonary vascular resistance (PVR). Blended with ventilatory gases and titrated to effect. Typical starting dose is 20 parts per million (ppm). Unlikely to be efficacious  $>40$  ppm. Complications include methemoglobinemia (reduce NO dose for methemoglobin  $>4\%$ ),  $NO_2$  poisoning (reduce NO dose for  $NO_2$  concentration  $>1\text{--}2$  ppm).
    - (2) Prostaglandin  $I_2$  (prostacyclin): A complex molecule made from arachidonic acid; major endogenous pulmonary vasodilator. Normally produced by lung when lung vessels are constricted.
  - e. **Broad-spectrum antibiotics:** Sepsis is a common underlying cause of PPHN.
  - f. **Consider extracorporeal membrane oxygenation (ECMO):** Reserved for cases of severe cardiovascular instability, oxygenation index (OI)  $> 40$  for  $>3$  hour, or alveolar-arterial gradient ( $A\text{--}a_{O_2}$ )  $\geq 610$  for 8 hours (see Chapter 4 for calculation of OI and  $A\text{--}a_{O_2}$ .  $P_{aO_2}$  should be postductal).

Patients typically need to be >2000 g and >34 weeks' gestation; should have head ultrasound and echocardiogram before initiating ECMO.

4. **Mortality depends on underlying diagnosis:** Mortality rates generally lower for RDS and meconium aspiration but higher in sepsis and diaphragmatic hernia.

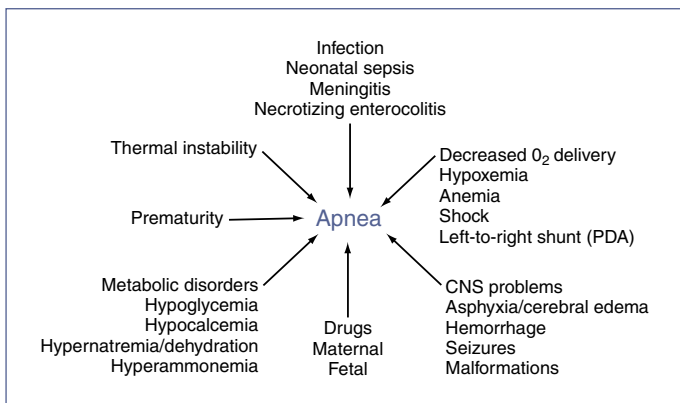
#### D. Spontaneous Pneumothorax

1. Seen in 1%–2% of normal newborns.
2. Associated with use of high inspiratory pressures and underlying diseases such as RDS, meconium aspiration, and pneumonia.
3. Patient should be monitored in a neonatal intensive care unit (NICU) setting.

### VIII. APNEA AND BRADYCARDIA

#### A. Apnea<sup>7</sup>

1. **Definition:** Respiratory pause > 20 seconds, or a shorter pause associated with cyanosis, pallor, hypotonia, or bradycardia < 100 bpm. In preterm infants, apnea may be central (no diaphragmatic activity), obstructive (upper airway obstruction), or mixed central and obstructive. Common causes of apnea in the newborn are listed in [Figure 18-5](#).
2. **Incidence:** Apnea of prematurity occurs in most infants born at <28 weeks' gestation, ≈50% of infants born at 30–32 weeks' gestation, and <7% of infants born at 34–35 weeks' gestation. Usually resolves by 34–36 weeks' postconceptual age but may persist after term in infants born at <25 weeks' gestation.



**FIGURE 18-5**

Causes of apnea in the newborn. CNS, Central nervous system; PDA, patent ductus arteriosus. (From Klaus MH, Fanaroff AA. *Care of the High-Risk Neonate*. 5th ed. Philadelphia: WB Saunders, 2001:268.)

### 3. Management:

- a. Consider pathologic causes for apnea.
- b. Pharmacotherapy with caffeine or other stimulants.
- c. Continuous positive airway pressure or mechanical ventilation (see Chapter 4 for details).

### B. Bradycardia Without Central Apnea

Etiologies include obstructive apnea, mechanical airway obstruction, gastroesophageal reflux, increased intracranial pressure (ICP), increased vagal tone (defecation, yawning, rectal stimulation, placement of nasogastric [NG] tube), electrolyte abnormalities, heart block.

## IX. CARDIAC DISEASES

### A. Patent Ductus Arteriosus (PDA)

1. **Definition:** Failure of ductus arteriosus to close in first few days of life, or reopening after functional closure. Typically results in left-to-right shunting of blood once PVR has decreased. If PVR remains high, blood may be shunted right to left, resulting in hypoxemia (see [Section VII.C](#)).
2. **Incidence:** Up to 60% in preterm infants weighing <1500 g, higher in those <1000 g. Female-to-male ratio is 2:1. Obligatory PDA is found in 10% of infants with congenital heart disease.
3. **Risk factors:** Most often related to hypoxia and immaturity. Term infants with PDA usually have structural defects in ductal vessel walls.
4. **Diagnosis:**
  - a. Examination: Systolic murmur that may be continuous, best heard at left upper sternal border or left infraclavicular area. May have apical diastolic rumble due to increased blood flow across mitral valve in diastole. Bounding peripheral pulses with widened pulse pressure if large shunt. Hyperactive precordium and palmar pulses may be present.
  - b. ECG: Normal or left ventricular hypertrophy in small to moderate PDA. Biventricular hypertrophy in large PDA.
  - c. Chest radiograph: May have cardiomegaly and increased pulmonary vascular markings, depending on size of shunt.
  - d. Echocardiogram.
5. **Management:**
  - a. Ongoing controversy over indications for treatment, timing of intervention, and best management strategy
  - b. Indomethacin: Prostaglandin synthetase inhibitor; 80% closure rate in preterm infants:
    - (1) For dosage information and contraindications, see Formulary.
    - (2) Complications: Transient decrease in glomerular filtration rate and decreased urine output, transient gastrointestinal bleeding (not associated with increased incidence of necrotizing enterocolitis [NEC]), prolonged bleeding time and disturbed platelet function for 7–9 days independent of platelet number (not associated with increased incidence of intracranial hemorrhage). Spontaneous

isolated intestinal perforations are seen with indomethacin use.  
Rates are higher with concomitant hydrocortisone use.

- c. Ibuprofen<sup>7,8</sup>: As effective as indomethacin but fewer renal adverse effects
- d. Surgical ligation of the duct

**B. Cyanotic Heart Disease**

See Chapter 7.

**X. HEMATOLOGIC DISEASES**

**A. Unconjugated Hyperbilirubinemia in the Newborn<sup>9</sup>**

- 1. **Overview:** During first 3–4 days of life, serum bilirubin increases from 1.5 mg/dL (cord blood) to  $6.5 \pm 2.5$  mg/dL:
  - a. Maximum rate of bilirubin increase for normal infants with nonhemolytic hyperbilirubinemia: 5 mg/dL/24 hr, or 0.2 mg/dL/hr
  - b. Consider pathologic cause: Visible jaundice or total bilirubin concentration > 5 mg/dL on first day of life
  - c. Risk factors: Birth weight < 2500 g, breast-feeding, prematurity
- 2. **Evaluation:**
  - a. Maternal prenatal testing: ABO and Rh (D) typing and serum screen for isoimmune antibodies
  - b. Infant or cord blood: Blood smear, direct Coombs test, blood and Rh typing (if maternal blood type is O, Rh negative, or prenatal blood typing was not performed)
- 3. **Management:**
  - a. Phototherapy: Ideally, intensive phototherapy should produce a decline of total serum bilirubin (TSB) level of 1–2 mg/dL within 4–6 hours, with further decline subsequently:
    - (1) Preterm newborn (Table 18-8)
    - (2) Term newborn (Fig. 18-6)
  - b. Intravenous immune globulin (IVIG) (>35 weeks' gestational age): In isoimmune hemolytic disease, IVIG administration (0.5–1 g/kg over 2 hours) is recommended if TSB is rising despite intensive phototherapy, or TSB level is within 2–3 mg/dL of exchange level. Repeat in 12 hours if needed.
  - c. Neonatal double-volume exchange transfusion (see Table 18-8 and Fig. 18-7):
    - (1) Volume: 160 mL/kg for full-term infant, 160–200 mL/kg for preterm infant.

TABLE 18-8		
GUIDELINES FOR USE OF PHOTOTHERAPY IN PRETERM INFANTS <1 WEEK OF AGE		
Weight (g)	Phototherapy (mg/dL)	Consider Exchange Transfusion (mg/dL)
500–1000	5–7	12–15
1000–1500	7–10	15–18
1500–2500	10–15	18–20
>2500	>15	>20

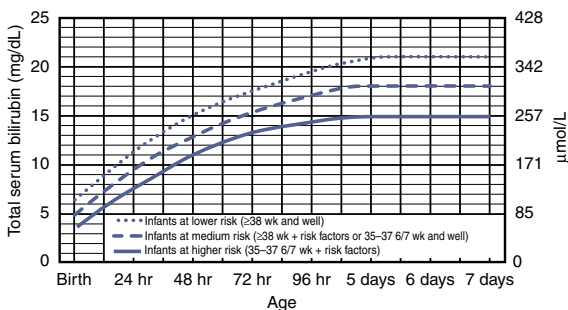


- (2) Route: During exchange, blood is removed through umbilical arterial catheter (UAC) and an equal volume is infused through umbilical venous catheter (UVC). If UAC is unavailable, use a single venous catheter.
- (3) Rate: Exchange in 15-mL increments for vigorous full-term infants. Exchange at 2–3 mL/kg/min in premature/less stable infants to avoid trauma to red blood cells.
- (4) Complications: Emboli, thromboses, hemodynamic instability, electrolyte disturbances, coagulopathy, infection, death.

**NOTE:** CBC, reticulocyte count, peripheral smear, bilirubin,  $\text{Ca}^{2+}$ , glucose, total protein, infant blood type, Coombs test, and newborn screen should be performed on a *preexchange sample* of blood; they are of no diagnostic value on postexchange blood. If indicated, save preexchange blood for serologic or chromosome studies.

## B. Conjugated Hyperbilirubinemia

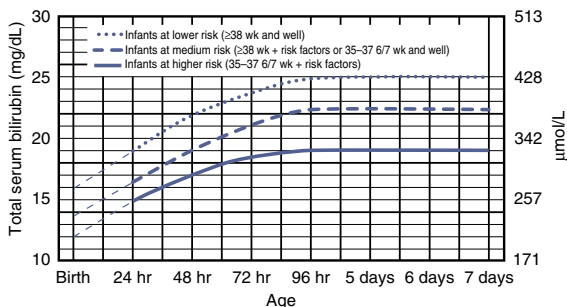
1. **Definition:** Direct bilirubin > 2.0 mg/dL and > 10% of TSB
2. **Etiology:** Biliary obstruction/atresia, choledochal cyst, hyperalimentation,  $\alpha_1$ -antitrypsin deficiency, hepatitis, sepsis, infections (especially urinary tract infections), hypothyroidism, inborn errors of metabolism, cystic fibrosis, red blood cell abnormalities



- Use total bilirubin. Do not subtract direct reacting or conjugated bilirubin.
- Risk factors: Isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis, or albumin < 3.0 g/dL (if measured).
- For well infants 35–37 6/7 wk can adjust TSB levels for intervention around the medium risk line. It is an option to intervene at lower TSB levels for infants closer to 35 wk and at higher TSB levels for those closer to 37 6/7 wk.
- It is an option to provide conventional phototherapy in hospital or at home at TSB levels 2–3 mg/dL (35–50 mmol/L) below those shown, but home phototherapy should not be used in any infant with risk factors.

**FIGURE 18-6**

Guidelines for phototherapy in infants born at 35 weeks' gestation or more. G6PD, Glucose-6-phosphate dehydrogenase; TSB, total serum bilirubin.



- The dashed lines for the first 24 hours indicate uncertainty due to a wide range of clinical circumstances and a range of responses to phototherapy.
- Immediate exchange transfusion is recommended if infant shows signs of acute bilirubin encephalopathy (hypertonia, arching, retrocollis, opisthotonos, fever, high-pitched cry) or if TBS is  $\geq 5$  mg/dL (85  $\mu$ mol/L) above these lines.
- Risk factors: Isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis.
- Measure serum albumin and calculate B/A ratio.
- Use total bilirubin. Do not subtract direct reacting or conjugated bilirubin.
- If infant is well and 35–37 6/7 wk (median risk) can individualize TSB levels for exchange based on actual gestational age.

**FIGURE 18-7**

Guidelines for exchange transfusion in infants born at 35 weeks' gestation or more. B/A, Bilirubin/Albumin; G6PD, glucose-6-phosphate dehydrogenase; TSB, total serum bilirubin.

3. **Management:** Ursodiol for infants on full feeds; consider supplementation with fat-soluble vitamins (A, D, E, K)

### C. Polycythemia

1. **Definition:** Venous hematocrit  $> 65\%$  confirmed on two consecutive samples. May be falsely elevated when sample obtained by heel stick. Arterial hematocrit samples may be lower and should not be used to evaluate polycythemia.
2. **Etiologies:** Delayed cord clamping, twin-twin transfusion, maternal-fetal transfusion, intrauterine hypoxia, Beckwith-Wiedemann syndrome, maternal gestational diabetes, neonatal thyrotoxicosis, congenital adrenal hyperplasia, trisomy 13, 18, or 21.
3. **Clinical findings:** Plethora, respiratory distress, cardiac failure, tachypnea, hypoglycemia, irritability, lethargy, seizures, apnea, jitteriness, poor feeding, thrombocytopenia, hyperbilirubinemia.
4. **Complications:** Hyperviscosity predisposes to venous thrombosis and CNS injury. Hypoglycemia may result from increased erythrocyte utilization of glucose.
5. **Management:** Partial exchange transfusion for symptomatic infants, with isovolemic replacement of blood with isotonic fluid. Blood is exchanged

in 10- to 20-mL increments to reduce hematocrit to <55. (See Chapter 14 to calculate amount of blood to be exchanged. Use birth weight (kg)  $\times$  90 mL/kg for estimated blood volume in mL.)

## XI. GASTROINTESTINAL DISEASES

### A. Necrotizing Enterocolitis

1. **Definition:** Serious intestinal inflammation and injury thought to be secondary to bowel ischemia, immaturity, and infection.
2. **Incidence:** More common in preterm (3%–4% of infants <2000 g) and African-American infants. Occurs principally in infants who have been fed.
3. **Risk factors:** Prematurity, asphyxia, hypotension, polycythemia-hyperviscosity syndrome, umbilical vessel catheterization, exchange transfusion, bacterial and viral pathogens, enteral feeds, PDA, congestive heart failure, cyanotic heart disease, RDS, intrauterine cocaine exposure.
4. **See Table EC 18-B:**
  - a. Systemic: Temperature instability, apnea, bradycardia, metabolic acidosis, hypotension, disseminated intravascular coagulopathy (DIC).
  - b. Intestinal: Elevated pregavage residuals with abdominal distention, blood in stool, absent bowel sounds, and/or abdominal tenderness or mass. Elevated pregavage residuals in the absence of other clinical symptoms rarely raise suspicion of NEC.
  - c. Radiologic: Ileus, intestinal pneumatosis, portal vein gas, ascites, pneumoperitoneum.
5. **Management:** Nothing by mouth, nasogastric tube decompression, maintain adequate hydration and perfusion, antibiotics for 7–14 days, surgical consultation. Surgery is performed for signs of perforation or necrotic bowel.

### B. Bilious Emesis Differential

See Table EC 18-C.

See Chapter 12.

1. **Mechanical:** Annular pancreas, intestinal atresia/duplication/malrotation/obstruction (including adjacent organomegaly), meconium plug or ileus, Hirschsprung, imperforate anus.
2. **Functional (i.e., poor motility):** NEC, electrolyte abnormalities, sepsis  
**NOTE:** Must eliminate malrotation as an etiology because its complication (volvulus) is a surgical emergency.

### C. Abdominal Wall Defects

See Table EC 18-D.

## XII. NEUROLOGIC DISEASES

### A. Intraventricular Hemorrhage (IVH)

1. **Definition:** Intracranial hemorrhage usually arising in the germinal matrix and periventricular regions of the brain.

TABLE EC 18-B

## MODIFIED BELL STAGING SYSTEM FOR NECROTIZING ENTEROCOLITIS (NEC)

Stage	Findings
IA (NEC suspected)	Temperature instability, apnea, bradycardia, lethargy, mild abdominal distention, gastric residuals, poor feeding, bilious emesis, occult blood in stool. X-ray findings: normal to mild ileus.
IB (NEC suspected)	As for Stage IA but with gross blood in stool
IIA (definite NEC, mildly ill)	As for stage IB, with pneumatosis intestinalis, absent bowel sounds $\pm$ abdominal tenderness
IIB (definite NEC, moderately ill)	As for Stage IIA, with metabolic acidosis, mild thrombocytopenia, definite abdominal tenderness, $\pm$ abdominal cellulitis or right lower quadrant mass, $\pm$ ascites or portal venous gas
IIIA (advanced NEC, severely ill infant, bowel intact)	As for stage IIB but with hypotension, bradycardia, apnea, metabolic and respiratory acidosis, neutropenia, disseminated intravascular coagulation, peritonitis, abdominal distention and tenderness, abdominal erythema, definite ascites
IIIB (severely ill, perforated bowel)	As for Stage IIIA, with pneumoperitoneum

Modified from Kleigman RM, Walsh MC. Neonatal necrotizing enterocolitis: pathogenesis, classification and spectrum of illness. *Curr Prob Pediatr*. 1987;17:219-288.

TABLE EC 18-C

## CONSIDERATIONS IN BILIOUS EMESIS

Pathophysiology	Bilious Emesis	
	Proximal Intestinal Obstruction	Distal Intestinal Obstruction
Differential diagnosis	Duodenal atresia Annular pancreas Malrotation with or without volvulus Jejunal obstruction/atresia	Ileal atresia Meconium ileus Colonic atresia Meconium plug: hypoplastic left colon syndrome Hirschsprung disease
Physical examination	Abdominal distention not prominent	Abdominal distention
Diagnosis	Abdominal x-ray: <i>double bubble</i> Upper gastrointestinal (GI) series	Abdominal x-ray: dilated loops of bowel Contrast enema Sweat test Mucosal rectal biopsy

TABLE EC 18-D

## DIFFERENCES BETWEEN OMPHALOCELE AND GASTROSCHISIS

	Omphalocele	Gastroschisis
Position	Central abdominal	Right paraumbilical
Hernia sac	Present	Absent
Umbilical ring	Absent	Present
Umbilical cord insertion	At vertex of sac	Normal
Herniation of other viscera	Common	Rare
Extraintestinal anomalies	Frequent	Rare
Intestinal infarction, atresia	Less frequent	More frequent

**2. Incidence:**

- a. 30%–40% of infants <1500 g; 50%–60% of infants <1000 g
- b. Highest incidence in first 72 hours of life: 60% within 24 hours, 85% within 72 hours, <5% after 1 week of age

**3. Diagnosis and classification:** Ultrasonography; grade is based on maximum amount of hemorrhage seen by age 2 weeks:

- a. Grade I: Hemorrhage in germinal matrix only
- b. Grade II: IVH without ventricular dilation
- c. Grade III: IVH with ventricular dilation (30%–45% incidence of motor and cognitive impairment)
- d. Grade IV: IVH with periventricular hemorrhagic infarct (60%–80% incidence of motor and cognitive impairment)

**4. Screening:** Indicated in infants <32 weeks' gestational age within first week of life; repeat in second week.**5. Prophylaxis:** Maintain acid-base balance and avoid fluctuations in blood pressure. Indomethacin is considered for IVH prophylaxis in some newborns (<28 weeks' gestation, birth weight <1250 g) and is most efficacious if given in first 6 hours of life, but has not been shown to impact long-term outcome.<sup>10</sup>**6. Outcome:** Infants with grade III and IV hemorrhages have a higher incidence of neurodevelopmental disabilities and an increased risk for posthemorrhagic hydrocephalus.**B. Periventricular Leukomalacia****1. Definition and ultrasound findings:** Ischemic necrosis of periventricular white matter, characterized by CNS depression within first week and ultrasound findings of cysts with or without ventricular enlargement caused by cerebral atrophy**2. Incidence:** More common in preterm infants but also occurs in term infants; 3.2% in infants <1500 g**3. Etiology:** Primarily ischemia-reperfusion injury, hypoxia, acidosis, hypoglycemia, acute hypotension, low cerebral blood flow**4. Outcome:** Commonly associated with cerebral palsy with or without sensory and cognitive deficit**C. Neonatal Seizures (See Chapter 20)****D. Neonatal Abstinence Syndrome**

Onset of symptoms usually occurs within first 24–72 hours of life (methadone may delay symptoms until 96 hours or later). Symptoms may last weeks to months. [Box 18-1](#) shows signs and symptoms of opiate withdrawal.

**E. Peripheral Nerve Injuries****1. Etiology:** Result from lateral traction on shoulder (vertex deliveries) or head (breech deliveries).**2. Clinical features (see [Table 18-9](#)).****3. Management:** Evaluate for associated trauma (clavicular and humeral fractures, shoulder dislocation, facial nerve injury, cord injuries). Full recovery is seen in 85%–95% of cases in first year of life.

## BOX 18-1

## OPIATE WITHDRAWAL

## Signs and Symptoms of Opiate Withdrawal

W	Wakefulness
I	Irritability, insomnia
T	Tremors, temperature variation, tachypnea, twitching (jitteriness)
H	Hyperactivity, high-pitched cry, hiccoughs, hyperreflexia, hypertonia
D	Diarrhea (explosive), diaphoresis, disorganized suck
R	Rub marks, respiratory distress, rhinorrhea, regurgitation
A	Apnea, autonomic dysfunction
W	Weight loss
A	Alkalosis (respiratory)
L	Lacrimation (photophobia), lethargy
S	Seizures, sneezing, stuffy nose, sweating, sucking (nonproductive)

TABLE 18-9

## PLEXUS INJURIES

Plexus Injury	Spinal Level Involved	Clinical Features
Erb-Duchenne palsy (90% of cases)	C5–C6 Occasionally involves C4	Adduction and internal rotation of arm. Forearm is pronated; wrist is flexed. Diaphragm paralysis may occur if C4 is involved.
Total palsy (8%–9% of cases)	C5–T1 Occasionally involves C4	Upper arm, lower arm, and hand involved. Horner syndrome (ptosis, anhydrosis, and miosis) exists if T1 is involved.
Klumpke paralysis (<2% of cases)	C7–T1	Hand flaccid with little control. Horner syndrome if T1 is involved.

XIII. RETINOPATHY OF PREMATURITY (ROP)<sup>11</sup>

## A. Definition

Interruption of normal progression of retinal vascularization.

## B. Etiology

Exposure of the immature retina to high oxygen concentrations can result in vasoconstriction and obliteration of the retinal capillary network, followed by vasoproliferation. Risk is greatest in the most immature infants.

## C. Diagnosis—Dilated Funduscopy Examination

Dilated funduscopy examination should be performed in the following patients:

1. All infants born  $\leq 30$  weeks' gestation
2. Infants born  $> 30$  weeks' gestation with unstable clinical course, including those requiring cardiorespiratory support
3. Any infant with a birth weight  $\leq 1500$  grams

D. Timing<sup>12</sup>

1. For all infants  $\leq 27$  weeks' gestation at birth, initial ROP screening examination should be performed at 31 weeks' postmenstrual age.

2. For all infants  $\geq 28$  weeks' gestation at birth, initial ROP screening examination should be performed at 4 weeks chronologic age.
3. For infants born before 25 weeks' gestation, consider earlier screening at 6 weeks chronologic age (even if before 31 weeks' postmenstrual age) on the basis of severity of comorbidities. This may enable earlier detection and treatment of aggressive posterior ROP, which is a severe form of rapidly progressive ROP.

### E. Classification

#### 1. Stage:

- a. Stage 1: Demarcation line separates avascular from vascularized retina
- b. Stage 2: Ridge forms along demarcation line
- c. Stage 3: Extraretinal fibrovascular proliferation tissue forms on ridge
- d. Stage 4: Partial retinal detachment
- e. Stage 5: Total retinal detachment

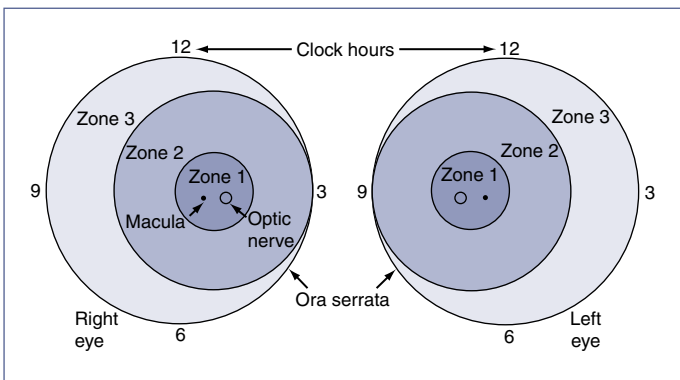
#### 2. Zone (Fig. 18-8)

3. **Plus disease:** Abnormal dilation and tortuosity of posterior retinal blood vessels in two or more quadrants of retina; may be present at any stage

#### 4. Number of clock hours or 30-degree sectors involved

### F. Management<sup>11</sup>

1. **Type 1 ROP:** Peripheral retinal ablation should be considered. Type 1 ROP classified as:
  - a. Zone I: Any stage ROP with plus disease
  - b. Zone I: Stage 3 ROP without plus disease
  - c. Zone II: Stage 2 or 3 ROP with plus disease



**FIGURE 18-8**

Zones of the retina. (From American Academy of Pediatrics. Screening examination of premature infants for retinopathy of prematurity, AAP policy statement. Pediatrics. 2013;131:189–195.)

2. **Type 2 ROP:** Serial examinations rather than retinal ablation should be considered. Type 2 ROP classified as:
  - a. Zone I: Stage 1 or 2 ROP without plus disease
  - b. Zone II: Stage 3 ROP without plus disease
3. **Follow-up** (Table 18-10)

**TABLE 18-10**
**SUGGESTED SCHEDULE FOR FOLLOW-UP OPHTHALMOLOGIC EXAMINATION IN RETINOPATHY OF PREMATURITY (ROP)**

≤1 Week	1–2 Weeks	2 Weeks	2–3 Weeks
Stage 1 or 2 ROP: zone I Stage 3 ROP: zone II	Stage 2 ROP: zone II Immature vascularization: posterior zone II	Stage 1 ROP: zone II	Stage 1 or 2 ROP: zone III
Immature vascularization: zone I, no ROP	Immature vascularization: posterior zone II	Immature vascularization: zone II, no ROP	Regressing ROP: zone III
Immature retina extends into posterior zone II near boundary of zone I	Unequivocally regressing ROP: zone I	Unequivocally regressing ROP: zone II	

**NOTE:** The presence of plus disease in zone I or II indicates that peripheral ablation rather than observation is appropriate.

From American Academy of Pediatrics. Screening examination of premature infants for retinopathy of prematurity, AAP policy statement. *Pediatrics*. 2013;131:189-195.

#### XIV. CONGENITAL INFECTIONS

See Chapter 17.

#### XV. COMMONLY USED MEDICATIONS IN THE NEONATAL INTENSIVE CARE UNIT (TABLE 18-11)

For neonatal specific drug dosing, refer to formulary or the Neofax.

**TABLE 18-11**
**DOSING OF COMMONLY USED ANTIBIOTICS IN THE NEONATAL INTENSIVE CARE UNIT, BASED ON POSTMATERNAL AND POSTNATAL AGE**

<b>AMPICILLIN</b> (GBS bacteremia = 150–200 mg/kg/day; GBS meningitis = 300–400 mg/kg/day)	<b>VANCOMYCIN</b> (bacteremia = 10 mg/kg/dose; meningitis = 15 mg/kg/dose)	<b>METRONIDAZOLE</b> <sup>†</sup> (loading = 15 mg/kg/dose; maintenance = 7.5 mg/kg/dose)
<b>CEFOTAXIME</b> 50 mg/kg/dose (gonococcal infections = 25 mg/kg/dose) (GC ophthalmia Ppx if maternal GC infection is present = 100 mg/kg × 1 dose)		
<b>OXACILLIN</b> 25–50 mg/kg/dose		

Continued



TABLE 18-11

## DOSING OF COMMONLY USED ANTIBIOTICS IN THE NEONATAL INTENSIVE CARE UNIT, BASED ON POSTMATERNAL AND POSTNATAL AGE—cont'd

Dosing Interval Chart			Dosing Interval Chart			Dosing Interval Chart		
PMA (weeks)	Postnatal (days)	Interval (hours)	PMA (weeks)	Postnatal (days)	Interval (hours)	PMA (weeks)	Postnatal (days)	Interval (hours)
≤29	0–28	12	≤29	0–14	18	≤29	0–28	48
	>28	8		>14	12		>28	24
30–36	0–14	12	30–36	0–14	12	30–36	0–14	24
	>14	8		>14	8		>14	12
37–44	0–7	12	37–44	0–7	12	37–44	0–7	24
	>7	8		>7	8		>7	12
≥45	All	6	≥45	All	6	≥45	All	8

## GENTAMICIN

## FLUCONAZOLE†

(Invasive candidiasis: loading = 12–25 mg/kg/dose; maintenance = 6–12 mg/kg/dose)

Dosing Chart				Dosing Interval Chart		
PMA (weeks)	Postnatal (days)	Dose (mg/kg)	Interval (hours)	Gest. Age (weeks)	Postnatal (days)	Interval (hours)
≤29*	0–7	5	48	≤29	0–14	48
	8–28	4	36		>14	24
	≥29	4	24	30 and older	0–7	48
30–34	0–7	4.5	36		>7	24
	≥8	4	24			
≥35	All	4	24			

\*Or significant asphyxia, PDA, or treatment with indomethacin.

†Thrush = 6 mg/kg/dose on day 1, then 3 mg/kg/dose orally (PO) Q24 hr, regardless of gestational or postnatal age.

GBS, Group B *Streptococcus*; GC, gonococcus; Gest., gestational; PDA, patent ductus arteriosus; PMA, postmaternal age; Ppx, prophylaxis.

Online Neofax: <http://neofax.thomsonhc.com/neofax/index.php>. 2010. Thomson Reuters Inc. • Application Version: 3.0.0.4 • User Manual Version: 200901.

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# Chapter 19

## Nephrology

*Katie Shaw, MD*

### I. WEBSITES

The International Pediatric Hypertension Association:

[www.pediatrichypertension.org](http://www.pediatrichypertension.org)

American Academy of Pediatrics (AAP) Urinary Tract Infection (UTI)

Practice Guidelines for Children 2–24 months: [UTI Guidelines 2011](#)

National Kidney Disease Education Program: [NKDEP Website](#)

National Kidney Foundation: [www.kidney.org](http://www.kidney.org)

### II. URINALYSIS, URINE DIPSTICK, AND MICROSCOPY

Urinalysis (UA) components are useful in clinical evaluation but rarely diagnostic in isolation. The clinician should be mindful of the possibility of false-positive and false-negative results, particularly with the dipstick, owing to a variety of factors.

Best if urine specimen is evaluated within 1 hour after voiding. Annual screening UAs are no longer recommended by the AAP.

#### A. Color

Normal urine varies in color from almost colorless to amber.

#### B. Turbidity

Cloudy urine can be normal; is most often the result of crystal formation at room temperature. Uric acid crystals form in acidic urine, and phosphate crystals form in alkaline urine. Cellular material and bacteria can also cause turbidity.

#### C. Specific Gravity

1. **Purpose:** Used as a measurement of a kidney's ability to concentrate urine. Easily determined surrogate of osmolality.
2. **Normal findings:** Between 1.003 and 1.030.
3. **Special circumstances:**
  - a. Isosthenuria: Excretion of urine with osmolality equal to plasma (neither concentrated or diluted). Typically a specific gravity of 1.010.
  - b. Disease states affecting the kidney's ability to concentrate urine may have a urine specific gravity fixed at 1.010 (i.e., chronic kidney disease).
  - c. Glucose, abundant protein, and iodine-containing contrast materials can give falsely high readings.

#### D. pH

1. **Purpose:** Used in determining the renal tubules' ability to maintain normal hydrogen ion concentration.
2. **Findings:** Normal ranges from 4.5–8, with an average range of 5–6.

**E. Protein**

1. **Purpose:** Used for screening and monitoring proteinuria. Should be quantified more precisely when needed for diagnostic purposes (see [Section VII](#) and related figures).
2. **Findings:** Dipstick provides readings of negative, trace, 1+ (~30 mg/dL), 2+ (~100 mg/dL), 3+ (~300 mg/dL), and 4+ (>1000 mg/dL).

**F. Sugars**

1. **Purpose:** Used to detect sugar in urine; glucosuria is always abnormal.
2. **Findings:** Glucosuria is suggestive but not diagnostic of diabetes mellitus or proximal renal tubular disease (see [Section VIII](#)). Blood level of glucose at which kidney tubular reabsorption is exceeded is typically between 160 and 180 mg/dL.
3. **Special circumstances:** Different tests are available to detect glucose/sugars. Reduction tests (e.g., Clinitest) will detect other sugars such as galactose, lactose, fructose, pentoses, and glucose. Enzyme tests (e.g., Clinistix) are specific for glucose only.

**G. Ketones**

1. **Purpose:** Used to detect altered metabolism by detecting breakdown of fatty acids and fats. Useful in patients with diabetes and altered carbohydrate metabolism.
2. **Findings:** Except for trace amounts, ketonuria suggest ketoacidosis, usually due to diabetes mellitus or catabolism induced by inadequate intake. Neonatal ketoacidosis may occur with metabolic defects (e.g., propionic acidemia, methylmalonic aciduria, glycogen storage disease).

**H. Nitrite**

See [Section III.E.1.a](#)

**I. Leukocyte Esterase**

See [Section III.E.1.b](#)

**J. Hemoglobin, Myoglobin**

1. **Purpose:** Used to detect glomerular or urologic injury.
2. **Findings:** Dipstick reads positive with intact red blood cells (as few as 3–4 red blood cells [RBCs]/high-powered field [hpf]), hemoglobin, or myoglobin. Hemoglobinuria is seen with intravascular hemolysis or in a hematuric urine that has been standing for an extended period. Myoglobinuria is seen in crush injuries, vigorous exercise, major motor seizures, fever, malignant hyperthermia, electrocution, snake bites, and ischemia.

**K. Bilirubin, Urobilinogen (Table 19-1)**

Dipstick measures each individually.

1. **Urine bilirubin:** Positive with conjugated hyperbilirubinemia; in this form, bilirubin is water soluble and excreted by the kidney.
2. **Urobilinogen:** Increased in all cases of hyperbilirubinemia where there is no obstruction to enterohepatic circulation.

**TABLE 19-1**  
**URINALYSIS FOR BILIRUBIN/UROBILINOGEN**

	Normal	Hemolytic Disease	Hepatic Disease	Biliary Obstruction
Urine urobilinogen	Normal	Increased	Increased	Decreased
Urine bilirubin	Negative	Negative	±	Positive

**L. Red Blood Cells (RBC)**

- Purpose:** Used to differentiate the presence of hemoglobinuria/myoglobinuria from intact RBCs.
- Findings:** Centrifuged urine normally contains <5 RBCs/hpf. Examination of RBC morphology may help localize the source of bleeding; dysmorphic RBCs suggest a glomerular origin, whereas normal RBCs suggest lower tract bleeding. See [Section VI](#) for further definitions and evaluation of persistent hematuria.

**M. White Blood Cells (WBC)**

- Purpose:** Used to detect infection or inflammation anywhere in the genitourinary tract.
- Findings:** ≥5 white blood cells (WBCs)/hpf of a properly spun urine specimen is suggestive of urinary tract infection (UTI). Relative to UTI, sterile pyuria is much less common in the pediatric population. If sterile pyuria is present, it is usually transient and accompanies systemic infectious or inflammatory disorders (e.g., Kawasaki disease).

**N. Epithelial Cells**

- Purpose:** Squamous epithelial cells are used as an index of possible contamination by vaginal secretions in females or by foreskin in uncircumcised males.
- Findings:** Any amount indicates possible contamination.

**O. Sediment**

Using light microscopy, unstained centrifuged urine can be examined for formed elements, including casts, cells, and crystals.

**P. Urine Gram Stain**

Gram stain is used to screen for UTIs. One organism per high-power field in uncentrifuged urine represents at least 10<sup>5</sup> colonies/mL.

**III. EVALUATION AND MANAGEMENT OF URINARY TRACT INFECTIONS**

**A. History**

Obtain voiding history (stool, urine), stream characteristics in toilet-trained children, sexual intercourse, sexual abuse, circumcision, masturbation, pinworms, prolonged baths, bubble baths, evaluation of growth curve, recent antibiotic use, and family history of vesicoureteral reflux (VUR), recurrent UTIs, or chronic kidney disease.

## B. Physical Examination

Vital signs, especially blood pressure, abdominal examination for flank masses, bowel distention, evidence of impaction, meatal stenosis or circumcision in males, vulvovaginitis or labial adhesions in females, neurologic examination of lower extremities, perineal sensation and reflexes, and rectal and sacral examination (for anteriorly placed anus).

## C. Risk Factors

Recent AAP guidelines for children 2–24 months provide resources to help clinicians stratify the risk of UTI in the absence of another source of infection in a febrile child.

1. **Females are at higher risk for UTI than males.**
2. **Uncircumcised males are at higher risk.**
3. **Other risk factors include nonblack race, fever  $\geq 39^{\circ}\text{C}$ , and fever  $>1\text{--}2$  days.**

## D. Method of Obtaining Urine Sample

1. **If a child is 2 months to 2 years of age, has a fever, and appears sufficiently ill to warrant immediate antibiotics**, obtain urinalysis and urine culture by transurethral catheterization.
2. **If a child is 2 months to 2 years of age, has a fever, and does not appear ill enough to warrant immediate antibiotics**, obtain urine by catheterization or the most convenient method available. If UA does not suggest UTI, it is reasonable to avoid antimicrobial therapy. If UA does suggest UTI, urine culture should be obtained by catheterization.

## E. Diagnosis

1. **To establish the diagnosis of UTI**, both urinalysis results suggestive of infection and positive urine culture are recommended.
- a. Nitrite test:
    - (1) Purpose: Used to detect nitrites produced by reduction of dietary nitrates by urinary gram-negative bacteria (especially *Escherichia coli*, *Klebsiella*, and *Proteus*).
    - (2) Findings: Positive test is strongly suggestive of a UTI because of high specificity. Nitrite sensitivity is 15%–82% and specificity is 90%–100%.
    - (3) Special circumstances: False-negative (low sensitivity) results commonly occur with insufficient time for conversion of urinary nitrates to nitrites (age-dependent voiding frequency) and inability of bacteria to reduce nitrates to nitrites (many gram-positive organisms such as *Enterococcus*, *Mycobacterium* spp., and fungi).
  - b. Leukocyte esterase test:
    - (1) Purpose: Used to detect esterases released from broken-down leukocytes. An indirect test for WBCs.
    - (2) Findings: Positive test is more sensitive (67%–84%) than specific (64%–92%) for a UTI.
  - c. Pyuria: Defined at a threshold of 5 WBCs/hpf. Absence of pyuria is rare if a true UTI is present.






## d. Urine culture:

- (1) Suprapubic aspiration: >50,000 colony-forming units (CFUs) necessary to diagnose a UTI. Some resources do consider <50,000 CFUs diagnostic of a UTI. Recommend clinical correlation.
- (2) Transurethral catheterization: >50,000 CFUs necessary to diagnose a UTI.
- (3) Clean catch: >100,000 CFUs necessary to diagnose a UTI.
- (4) Bagged specimen: Positive culture cannot be used to document a UTI.
- (5) Catheter Associated (indwelling urethral or suprapubic): No specific data for pediatric patients. Adult IDSA guidelines define as presence of symptoms and signs compatible with UTI and > 1000 CFU/mL of 1 or more bacterial species in a single catheter urine specimen or in a midstream voided urine specimen from patient whose catheter has been removed within previous 48 hours.<sup>2</sup>

**F. Culture-Positive UTI**

Treatment: Based on urine culture and sensitivities if possible; for empirical therapy, see Chapter 17.

1. **Upper versus lower UTI:** Fever, systemic symptoms, and costovertebral angle tenderness suggest pyelonephritis (upper UTI) rather than cystitis (lower UTI). Fever that persists for >48 hours after initiating appropriate antibiotics is also suggestive of pyelonephritis. Although a <sup>99m</sup>Tc-dimercaptosuccinic acid (DMSA) scan is the gold standard to diagnose pyelonephritis, infants with febrile UTI are assumed to have pyelonephritis and are treated as such.
2. **Organisms:** *E. coli* is the most common cause of pediatric UTI. Other common pathogens include *Klebsiella*, *Proteus* spp., *Staphylococcus saprophyticus*, and *Staphylococcus aureus*. Group B streptococci and other bloodborne pathogens are important in neonatal UTIs, whereas *Enterococcus* and *Pseudomonas* are more prevalent in abnormal hosts (e.g., recurrent UTI, abnormal anatomy, neurogenic bladder, hospitalized patients, or those with frequent bladder catheterizations).
3. **Treatment considerations:**
  - a. Hospitalize all febrile children age <4 weeks, and treat with intravenous (IV) antibiotics, owing to risk for bacteremia and meningitis.
  - b. Parenteral antibiotics for children who are toxic, dehydrated, or unable to tolerate oral medication due to vomiting or noncompliance. Studies comparing duration are inconclusive, but experts traditionally recommend 7–10 days for uncomplicated cases and 14 days for toxic children and those with pyelonephritis. Some recent studies have shown that 2–4 days of oral antibiotics in uncomplicated lower tract UTIs are as effective as 7–10 days of oral treatment.<sup>4</sup>
4. **Inadequate response to therapy:** Repeat urine culture in children with expected response is controversial but generally thought to be unnecessary. Repeat culture, as well as renal ultrasound to rule out an abscess or urinary obstruction, is indicated in children with poor response to

Grade I	Grade II	Grade III	Grade IV	Grade V
				
Ureter only	Ureter, pelvis, calyces; no dilatation, normal calyceal fornices	Mild or moderate dilatation and/or tortuosity of ureter; mild or moderate dilatation of the pelvis, but no or slight blunting of the fornices	Moderate dilatation and/or tortuosity of the ureter; mild dilatation of renal pelvis and calyces; complete obliteration of sharp angle of fornices, but maintenance of papillary impressions in majority of calyces	Gross dilatation and tortuosity of ureter; gross dilatation of renal pelvis and calyces; papillary impressions are no longer visible in majority of calyces

**FIGURE 19-1**

International classification of vesicoureteral reflux. (Modified from Rushton H. *Urinary tract infections in children: epidemiology, evaluation, and management*. *Pediatr Clin North Am.* 1997;44:5; and International Reflux Committee. *Medical vs. surgical treatment of primary vesicoureteral reflux: report of the International Reflux Study Committee*. *Pediatrics.* 1981;67:392.)

therapy. Repeat cultures should also be considered in patients with recurrent UTIs to rule out persistent bacteriuria.

##### 5. Imaging studies (Fig. 19-1):

- Anatomic evaluation: New guidelines for children aged 2–24 months continue to recommend obtaining an ultrasound of the kidneys and bladder after the first UTI is diagnosed. In a change from prior recommendations, a voiding cystourethrogram (VCUG) is recommended after a second UTI is diagnosed or as indicated by an abnormal kidney and bladder ultrasound (hydronephrosis, scarring, or other findings to suggest either high-grade vesicoureteral reflux [VUR] or obstructive uropathy).<sup>3</sup>
  - Kidney and Bladder Ultrasonography: To evaluate for gross structural defects, obstructive lesions, positional abnormalities, and kidney



size and growth. Should be done at the earliest convenient time unless the child fails to demonstrate expected clinical response, which should prompt a more immediate kidney sonogram.

- (2) VCUG: To evaluate bladder anatomy, emptying, and VUR. May be substituted with radionuclide cystogram (RNC), which has 1/100 the radiation exposure of VCUG and increased sensitivity for transient reflux. RNC does not visualize urethral anatomy, is not sensitive for low-grade reflux, and cannot grade reflux.
  - b. Abdominal radiograph: If indicated, to evaluate stool pattern and for spinal dysraphism.
  - c. Dimercaptosuccinic acid (DMSA):  $^{99m}\text{Tc}$ -DMSA scan can detect areas of decreased uptake that may represent acute pyelonephritis or chronic kidney scarring; does not differentiate between the two. Routine use not recommended; may be indicated in patients with an abnormal VCUG or kidney sonography, in patients with history of asymptomatic bacteriuria and fever. Repeat in 3–6 months if initial study is positive to evaluate for persistent infection and kidney scarring if clinically indicated.
  - d. Diethylenetriamine pentaacetic acid (DTPA)/mercaptoacetyl triglycine (MAG-3): In the setting of hydronephrosis, can be used to assess drainage of the urinary collecting system to characterize possible upper urologic tract obstructions at ureteropelvic or ureterovesico junction. May also be used for indications given above for DMSA.
6. **Management of VUR:**
- a. Antibiotic prophylaxis: Conventionally, low-dose antibiotic prophylaxis has been recommended in all children with VUR and obstructive disease. New guidelines call into question the efficacy of antibiotic prophylaxis in preventing UTI and subsequent kidney disease in the setting of VUR; studies are ongoing to determine its role.<sup>5-7</sup> The Randomized Intervention for the Management of Vesicoureteral Reflux (RIVUR) Study is a randomized double-blinded controlled clinical trial (only in the United States) aiming to answer the question of antibiotic prophylaxis necessity and results are anticipated in 2014 after the publication of this edition.
  - b. Surgical intervention: Persistence/grade of VUR is typically monitored yearly, often in consultation with a pediatric urologist. Higher-grade VUR that persists as the child grows may ultimately require surgical intervention, the timing of which may be affected by factors such as presence of bilateral VUR, kidney/scarring, other underlying urologic disease, recurrent kidney infections, and/or ease of family follow-up. No model predicting the resolution of VUR has been verified.
  7. **Asymptomatic bacteriuria:** Defined as bacteria in urine on microscopy and Gram stain in an afebrile, asymptomatic patient without pyuria. Antibiotics not necessary if voiding habits and urinary tract are normal. DMSA may be helpful in differentiating pyelonephritis from fever and coincidental bacteriuria.
  8. **Referral to pediatric urology:** Consider in children with abnormal voiding patterns based on history or imaging, neurogenic bladder, abnormal anatomy, recurrent UTI, or poor response to appropriate antibiotics.

TABLE 19-2

## NORMAL VALUES OF GLOMERULAR FILTRATION RATE

Age	GFR (Mean) (mL/min/1.73 m <sup>2</sup> )	Range (mL/min/1.73 m <sup>2</sup> )
Neonates <34 wk gestational age		
2–8 days	11	11–15
4–28 days	20	15–28
30–90 days	50	40–65
Neonates >34 wk gestational age		
2–8 days	39	17–60
4–28 days	47	26–68
30–90 days	58	30–86
1–6 mo	77	39–114
6–12 mo	103	49–157
12–19 mo	127	62–191
2 yr–adult	127	89–165

From Holliday MA, Barratt TM. *Pediatric Nephrology*. Baltimore: Williams & Wilkins, 1994:1306.

## IV. KIDNEY FUNCTION TESTS

## A. Tests of Glomerular Function

- Glomerulogenesis is complete at 36 weeks' gestation.** Glomerular filtration rate (GFR) increases over the first few years of life related to glomerular maturation.
- Normal GFR values as measured by inulin clearance (gold standard)** are shown in Table 19-2.
- Creatinine clearance (CCr):**  
Timed urine specimen: Standard measure of GFR; closely approximates inulin clearance in the normal range of GFR. When GFR is low, CCr overestimates GFR. Usually inaccurate in children with obstructive uropathy or problems with bladder emptying.

$$\text{CCr (mL/min/1.73 m}^2\text{)} = (U \times [V/P]) \times 1.73/\text{BSA},$$

where  $U$  (mg/dL) = urinary creatinine concentration;  $V$  (mL/min) = total urine volume (mL) divided by the duration of the collection (min) (24 hours = 1440 min);  $P$  (mg/dL) = serum creatinine concentration (may average two levels); and  $\text{BSA (m}^2\text{)}$  = body surface area.

- Estimated GFR (eGFR) from plasma creatinine:** Convenient estimate of kidney function in clinical venue as challenging to determine if creatinine is normal, given variation related to body size/muscle mass. If body habitus is markedly abnormal or precise measurement of GFR is needed, consider determining GFR by methods other than estimation. Creatinine must be in steady state to estimate GFR; use caution in the setting of acute kidney injury. Two equations to calculate estimated GFR:
  - Bedside Chronic Kidney Disease in Children (CKiD) cohort: Newly developed equation based on current laboratory methodologies to determine creatinine. Recommended for eGFR determination in children aged 1–16 years. Estimated GFRs of  $\geq 75$  mL/min/1.73 m<sup>2</sup> determined by this

**TABLE 19-3**  
**PROPORTIONALITY CONSTANT FOR CALCULATING GLOMERULAR FILTRATION RATE**

Age	k Values
Low birth weight during first year of life	0.33
Term AGA during first year of life	0.45
Children and adolescent girls	0.55
Adolescent boys	0.70

AGA, Appropriate for gestational age.  
 Data from Schwartz GJ, Brion LP, Spitzer A. The use of plasma creatinine concentration for estimating glomerular filtration rate in infants, children, and adolescents. *Pediatr Clin North Am.* 1987;34:571.

equation likely represent normal kidney function; clinical correlation is recommended as always with GFR estimation.<sup>8</sup>

$$\text{eGFR (mL/min/1.73 m}^2\text{)} = 0.413 \times (L/P_{\text{Cr}}),$$

where 0.413 is proportionality constant,  $L$  = height (cm), and  $P_{\text{Cr}}$  = plasma creatinine (mg/dL).

- b. Schwartz equation: Traditional equation for eGFR. However, given changes in laboratory assays used to determine creatinine, this equation systemically overestimates GFR and should be considered when applying clinically:

$$\text{eGFR (mL/min/1.73 m}^2\text{)} = kL/P_{\text{Cr}},$$

where  $k$  = proportionality constant;  $L$  = height (cm); and  $P_{\text{Cr}}$  = plasma creatinine (mg/dL) (Table 19-3).

- c. Modification of Diet in Renal Disease (MDRD) and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI): Used to calculate GFR in those > 18 years old. (See NKDEP website.)
- 5. **Other measurements of GFR:** May be used when more precise determination of GFR is needed (e.g., dosing of chemotherapy). These methods include iothalamate, DTPA, and iohexol.

**B. Tests of Kidney Tubular Function**

**1. Proximal tubule:**

- a. Proximal tubule reabsorption: Proximal tubule is responsible for reabsorption of electrolytes, glucose, and amino acids. Studies to evaluate proximal tubular function compare urine and blood levels of specific compounds, arriving at a percentage of tubular reabsorption (Tx):

$$\text{Tx} = 1 - [(U_x/P_x)/(U_{\text{Cr}}/P_{\text{Cr}})] \times 100\%,$$

where  $U_x$  = concentration of compound in urine;  $P_x$  = concentration of compound in plasma;  $U_{\text{Cr}}$  = concentration of creatinine in urine; and  $P_{\text{Cr}}$  = concentration of creatinine in plasma. This formula can be used for amino acids, electrolytes, calcium, and phosphorus. For example, in the setting of hypophosphatemia, tubular reabsorption of phosphorus near 100% would be expected in a kidney with preserved proximal tubular function.

- b. Calculation of fractional excretion of sodium (FENa) is derived from the equation<sup>9</sup>:

$$\text{FENa} = [(\text{UNa}/\text{PNa})/(\text{UCr}/\text{PCr})] \times 100\%.$$

FENa is usually <1% in prerenal azotemia or glomerulonephritis and >1% (usually >3%) in acute tubular necrosis (ATN) or postrenal azotemia. Infants have diminished ability to reabsorb sodium; FENa in volume-depleted infants is <3%. Recent diuretic use may give inaccurate results. A fractional excretion of urea (FEurea) may be useful in certain clinical scenarios:

$$\text{FEurea} = [(\text{Uurea}/\text{Purea})/(\text{UCr}/\text{PCr})] \times 100\%$$

FEurea is usually <35% in prerenal azotemia and >50% in ATN.<sup>9</sup>

- c. Glucose reabsorption: Glucosuria must be interpreted in relation to simultaneously determined plasma glucose concentration. If plasma glucose concentration is <160 mg/dL and glucose is present in urine, this implies abnormal tubular reabsorption of glucose and proximal renal tubular disease (see Section II.F).
- d. Bicarbonate reabsorption: Majority occurs in proximal tubule. Abnormalities in reabsorption lead to type 2 renal tubular acidosis (RTA; see Table 19-9).

## 2. Distal tubule:

- a. Urine acidification: A urine acidification defect (distal RTA) should be suspected when random urine pH values are >6 in the presence of moderate systemic metabolic acidosis. Confirm acidification defects by simultaneous venous or arterial pH, plasma bicarbonate concentration, and determination of the pH of fresh urine.
- b. Urine concentration occurs in the distal tubule: Urine osmolality, ideally on a first morning urine specimen, can be used to evaluate capacity to concentrate urine. (For more formal testing, see the water deprivation test in Chapter 10.)
- c. Urine calcium: Hypercalciuria may be seen with distal RTA, vitamin D intoxication, hyperparathyroidism, immobilization, excessive calcium intake, use of steroids or loop diuretics, or idiopathic. Diagnosis is as follows:
- (1) 24-hour urine: Calcium > 4 mg/kg/24 hr (gold standard)
  - (2) Spot urine: Determine calcium/creatinine (Ca/Cr) ratio. Normal urine Ca/Cr ratio does not rule out hypercalciuria. Correlate clinically and follow elevated spot urine Ca/Cr ratio with a 24-hr urine calcium determination if indicated (Table 19-4).<sup>10</sup>

**TABLE 19-4**

### AGE-ADJUSTED CALCIUM/CREATININE RATIOS

Age	Ca <sup>2+</sup> /Cr Ratio (mg/mg) (95th Percentile for Age)
<7 mo	0.86
7–18 mo	0.60
19 mo–6 yr	0.42
Adults	0.22

From Sargent JD, Stukel TA, Kresel J, et al. Normal values for random urinary calcium-to-creatinine ratios in infancy. *J Pediatr*. 1993;123:393.

V. ACUTE KIDNEY INJURY

A. Definition

Sudden decline in kidney function, clinically represented by rising creatinine, with or without changes in urine output.

B. Etiology (Table 19-5)

Causes are generally subdivided into three categories:

- Prerenal:** Impaired perfusion of kidneys, the most common cause of acute kidney injury (AKI) in children. Volume depletion is a common cause of prerenal AKI.
- Renal:**
  - Parenchymal disease due to vascular or glomerular lesions
  - ATN: Typically a diagnosis of exclusion when no evidence of renal parenchymal disease is present and prerenal and postrenal causes have been eliminated if possible
- Postrenal:** Obstruction of the urinary tract, commonly due to inherited anatomic abnormalities

TABLE 19-5  
ETIOLOGIES OF ACUTE KIDNEY INJURY

Prerenal	<p><b>Decreased true intravascular volume:</b> e.g., hemorrhage, volume depletion, sepsis, burns</p> <p><b>Decreased effective intravascular volume:</b> e.g., congestive heart failure, hepatorenal syndrome</p> <p><b>Altered glomerular hemodynamics:</b> e.g., NSAIDs, ACE inhibitors (when renal perfusion is already low)</p>
Intrinsic renal	<p><b>Acute tubular necrosis:</b></p> <p><i>Hypoxic/ischemic insults</i></p> <p><i>Drug-induced</i>—aminoglycosides, amphotericin B, acyclovir, chemotherapeutic agents (ifosfomide, cisplatin)</p> <p><i>Toxin-mediated</i>—endogenous toxins (myoglobin, hemoglobin); exogenous toxins (ethylene glycol, methanol)</p> <p><b>Interstitial nephritis:</b></p> <p><i>Drug-induced</i>—β-lactams, NSAIDs (may be associated with high-grade proteinuria), sulfonamides, PPIs</p> <p><i>Idiopathic</i></p> <p><b>Uric acid nephropathy</b> (tumor lysis syndrome)</p> <p><b>Glomerulonephritis:</b> In most severe degree, presents as rapidly progressive glomerulonephritis (RPGN)</p> <p><b>Vascular lesions:</b> Renal artery thrombosis, renal vein thrombosis, cortical necrosis, hemolytic uremic syndrome</p> <p><b>Hypoplasia/dysplasia:</b> idiopathic or exposure to nephrotoxic drug in utero</p>
Postrenal	<p><b>Obstruction in a solitary kidney</b></p> <p><b>Bilateral ureteral obstruction</b></p> <p><b>Urethral obstruction</b></p> <p><b>Bladder dysfunction</b></p>

ACE, Angiotensin-converting enzyme; NSAIDs, nonsteroidal antiinflammatory drugs; PPIs, proton pump inhibitors.  
Data from Andreoli SP. Acute kidney injury in children. *Pediatr Nephrol.* 2009;24:253-263.

### C. Clinical Presentation

Pallor, decreased urine output, edema, hypertension, vomiting, and lethargy. The hallmark of early kidney failure is often oliguria.

1. **Oliguria:** Urine output  $<300 \text{ mL/m}^2/24 \text{ hr}$ , or  $<0.5 \text{ mL/kg/hr}$  in children and  $<1.0 \text{ mL/kg/hr}$  in infants. May be an appropriate physiologic response to water depletion (prerenal state) or a reflection of intrinsic or obstructive kidney disease.
- a. Blood urea nitrogen/creatinine (BUN/Cr) ratio (both in mg/dL): Interpret ratios with caution in small children with low serum creatinines
  - (1) 10–20 (normal ratio): Suggests intrinsic renal disease in the setting of oliguria
  - (2)  $>20$ : Suggests volume depletion, prerenal azotemia, or gastrointestinal bleeding
  - (3)  $<5$ : Suggests liver disease, starvation, inborn error of metabolism
- b. Laboratory differentiation of oliguria (Table 19-6)

### D. Acute Tubular Necrosis

Clinically defined by three phases:

1. **Oliguric phase:** Period of severe oliguria that may last days. If oliguria or anuria persists for longer than 3–6 weeks, kidney recovery from ATN is less likely.
2. **High urine output phase:** Begins with increased urine output and progresses to passage of large volumes of isosthenuric urine containing sodium levels of 80–150 mEq/L.
3. **Recovery phase:** Signs and symptoms usually resolve rapidly, but polyuria may persist for days to weeks.

### E. Treatment Considerations

1. **Placement of indwelling catheter to monitor urine output.**
2. **Prerenal and postrenal factors** should be excluded and intravascular volume maintained with appropriate fluids in consultation with a pediatric nephrologist.

### F. Complications

Often dependent on clinical severity; usually includes fluid overload (hypertension, congestive heart failure [CHF], pulmonary edema), electrolyte disturbances (hyperkalemia), metabolic acidosis, hyperphosphatemia, and uremia.

TABLE 19-6

LABORATORY DIFFERENTIATION OF OLIGURIA

Test	Prerenal	Renal
FENa	$\leq 1\%$	$>3\%$
BUN/Cr ratio	$>20:1$	$<10:1$
Urine specific gravity	$>1.015$	$<1.010$

## G. Acute Dialysis

### 1. Indications:

When metabolic or fluid derangements are not controlled by aggressive medical management alone. Generally accepted criteria include the following, although a nephrologist should always be consulted:

- a. **Acidosis:** Intractable metabolic acidosis.
- b. Electrolyte abnormalities: Hyperkalemia  $>6.5$  mEq/L despite restriction of delivery and medical management. Calcium and phosphorus imbalance (e.g., hypocalcemia with tetany, seizures in the presence of a very high serum phosphate level). Derangements implicated in neurologic abnormalities.
- c. Ingestions or accumulation of dialyzable toxin or poison: Lithium, ammonia, alcohol, barbiturates, ethylene glycol, isopropanol, methanol, salicylates, theophylline. When available, poison control centers can provide guidance and expertise.
- d. Volume overload: Evidence of pulmonary edema or hypertension.
- e. Uremia: BUN  $>150$  mg/dL (lower if rising rapidly), uremic pericardial effusion, neurologic symptoms.

### 2. Techniques:

- a. Peritoneal dialysis: Requires catheter to access peritoneal cavity, as well as adequate peritoneal perfusion. May be used acutely or chronically.
- b. Intermittent hemodialysis: Requires placement of special vascular access catheters. May be method of choice for certain toxins (e.g., ammonia, uric acid, poisons) or when there are contraindications to peritoneal dialysis.
- c. Continuous arteriovenous hemofiltration/hemodialysis (CAVH/D) and continuous venovenous hemofiltration/hemodialysis (CVVH/D):
  - (1) Requires special vascular access catheter.
  - (2) Lower efficiency of solute removal compared with intermittent hemodialysis, but higher efficiency is not necessary because of the continuous nature of this form of dialysis.
  - (3) Sustained nature of dialysis allows for more gradual removal of volume/solutes, which is ideal for patients with hemodynamic or respiratory instability.

## VI. HEMATURIA AND ASSOCIATED DISORDERS 3,14

### A. Definitions

1. **Gross hematuria:** Blood in urine visible to the naked eye.
2. **Microscopic hematuria:** Blood not visible to naked eye, but  $\geq 5$  red blood cells per high-power field (RBCs/hpf).
3. **Red urine that is not hematuria:** Hemoglobinuria, myoglobinuria, brick dust urine (precipitated urates in typically acidic urine of neonates).
4. **Persistent hematuria:** Three positive urinalyses, based on dipstick and microscopic examination over at least a 2- to 3-week period, warranting further evaluation.
5. **Extraglomerular hematuria:** No RBC casts, minimal if any proteinuria.

TABLE 19-7

## CAUSES OF HEMATURIA IN CHILDREN

Kidney-related disease	Isolated glomerular disease	IgA nephropathy, Alport syndrome, thin glomerular basement membrane nephropathy, postinfectious/poststreptococcal glomerulonephritis, membranous nephropathy, membranoproliferative glomerulonephritis, focal segmental glomerulosclerosis, antiglomerular basement membrane disease
	Multisystem disease involving glomerulus	Systemic lupus erythematosus nephritis, Henoch-Schönlein purpura nephritis, granulomatosis with polyangiitis, polyarteritis nodosa, Goodpasture syndrome, hemolytic-uremic syndrome, sickle cell glomerulopathy, HIV nephropathy
	Tubulointerstitial disease	Pyelonephritis, interstitial nephritis, papillary necrosis, acute tubular necrosis
	Vascular	Arterial or venous thrombosis, malformations (aneurysms, hemangiomas), nutcracker syndrome, hemoglobinopathy (sickle cell trait/disease)
Urinary tract disease	Anatomic	Hydronephrosis, cystic kidney disease, polycystic kidney disease, multicystic dysplasia, tumor, trauma
		Inflammation (cystitis, urethritis) Urolithiasis Trauma Coagulopathy Arteriovenous malformations (AVMs) Bladder tumor Factitious syndrome

Data from Kliegman RM, Stanton BF, St. Geme JW, et al. *Nelson Textbook of Pediatrics*. 19th ed. Philadelphia: Saunders; 2011:1779.

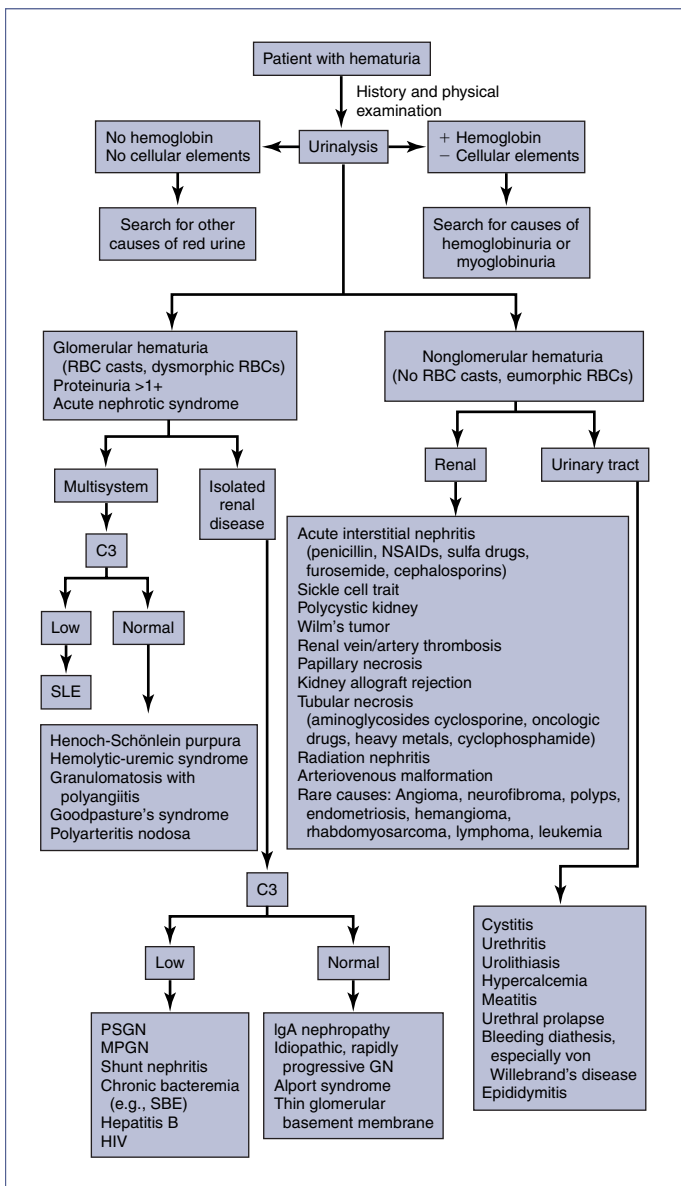
6. **Glomerular hematuria:** Most often tea-colored urine but may be red/pink, RBC casts, dysmorphic RBCs, associated with proteinuria.
7. **Acute nephritic syndrome:** Classically tea-colored urine, facial or body edema, hypertension, and oliguria.

## B. Etiologies (Table 19-7)

## C. Evaluation (Fig. 19-2)

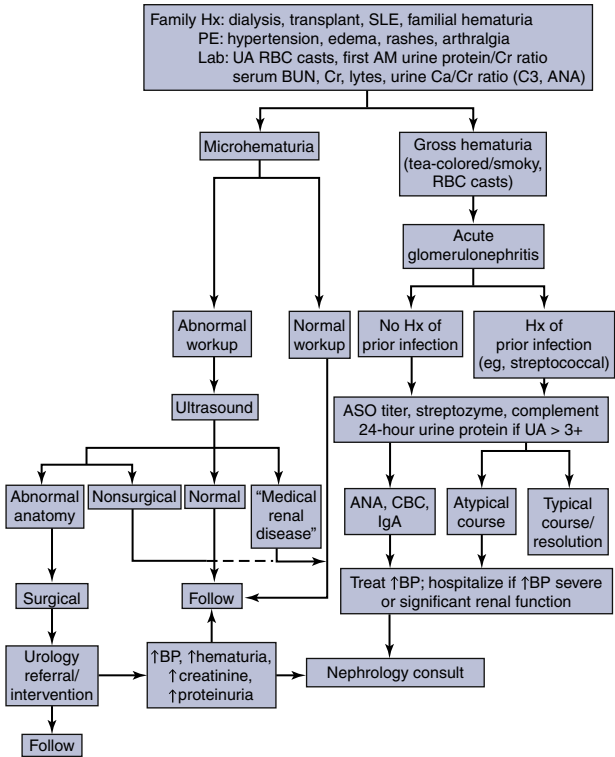
1. **Differentiate glomerular and extraglomerular hematuria:** Examine urine sediment looking for RBC casts and protein.
  - a. Glomerular hematuria
    - (1) Determine whether isolated kidney disease or multisystem disease: Complete blood cell count (CBC) with differential and smear, serum electrolytes with Ca, BUN/Cr, serum protein/albumin, and other testing driven by history and exam, including ANA, hepatitis B and C serologies, HIV, family history, audiology screen if indicated.
    - (2) Consider other studies to determine underlying diagnosis: C3/C4, antineutrophil antibody (c- and p-ANCA), anti-double-stranded DNA





**FIGURE 19-2**

Diagnostic strategy for hematuria. GN, Glomerulonephritis; HIV, human immunodeficiency virus; MPGN, membranoproliferative glomerulonephritis; NSAIDs, nonsteroidal antiinflammatory drugs; PSGN, poststreptococcal glomerulonephritis; RBC, red blood cell; SBE, subacute bacterial endocarditis; SLE, systemic lupus erythematosus.

**FIGURE 19-3**

Management algorithm for hematuria. (Data from Hay WM, Levin MJ, Deterding RR, Azbug MJ, Sondheimer JM. CURRENT Diagnosis & Treatment Pediatrics. 21st edition. Available at [www.accessmedicine.com](http://www.accessmedicine.com), Figure 24-1.

#### b. Extraglomerular hematuria

- (1) Rule out infection: Urine culture, gonorrhea, chlamydia
- (2) Rule out trauma: History, consider imaging of abdomen/pelvis
- (3) Investigate other potential causes: urine Ca/Cr ratio or 24-hour urine for kidney stone risk analysis, sickle cell screen, kidney/bladder ultrasound. Consider serum electrolytes with Ca, consider prothrombin time/partial thromboplastin time (PT/PTT).

#### D. Management (Fig. 19-3)

**VII. PROTEINURIA AND ASSOCIATED DISORDERS 14.15****A. Methods of Detection**

1. **Urinalysis:** See [Section II.E](#). Proteinuria on a urine dipstick should be verified by a protein/creatinine ratio in an appropriately collected first morning urine specimen.
2. **First morning urine protein/creatinine ratio:** Approximates 24-hour urine collections well and has additional benefit of minimizing detection of proteinuria from orthostatic proteinuria.  
Appropriate collection of a first morning urine sample is very important for accurate results. A child must empty the bladder before going to bed. If the child gets up during the night, they should empty their bladder before returning to bed. When the child wakes up in the morning, they should provide a urine sample immediately.
- a. Normal ratios:
  - (1) <2 years old: <0.5 mg/mg
  - (2) >2 years old: <0.2 mg/mg
- b. Abnormal ratios (mg/mg): Significant proteinuria detected on a first morning protein/creatinine ratio should prompt verification of appropriate collection. Repeat specimen should be analyzed within 1–2 weeks, or sooner based on clinical scenario (e.g., edema, hypertension, or symptom of concern would prompt a more expedited workup).
3. **24-hour urine protein:** Can have a contribution from benign orthostatic proteinuria, which cannot be ruled out without a fractional urine collection. Protein level >4 mg/m<sup>2</sup>/hr is considered significant.

**B. Definitions**

1. **Orthostatic proteinuria:** Excretion of insignificant amounts of protein in the supine position, but in the standing position, protein excretion increases to significant range. A benign condition and common cause of proteinuria in children and adolescents.
2. **Fixed proteinuria:** Proteinuria found on first morning urine void over several consecutive days. Suggestive of kidney disease.
3. **Microalbuminuria:** Presence of albumin in urine below detectable range of dipsticks. In adults, defined as 30–300 mg/g creatinine. Most often used in screening for kidney disease secondary to diabetes.
4. **Significant proteinuria:** UPr:UCr ratio 0.2–2.0 mg/mg or 4–40 mg/m<sup>2</sup>/hr in a 24-hour collection.
5. **Nephrotic-range proteinuria:** UPr:UCr ratio >2 mg/mg or >40 mg/m<sup>2</sup>/hr in a 24-hour collection. In adults, 24-hour urine protein excretion of 3000 mg/24 hr.
6. **Nephrotic syndrome:** Nephrotic-range proteinuria, hypoalbuminemia, and edema. Also associated with hyperlipidemia (cholesterol >200 mg/dL).

**C. Etiologies (Box 19-1)**

See [Section VII.E](#) for information about nephrotic syndrome.

## BOX 19-1

## CAUSES OF PROTEINURIA

**Transient proteinuria:** Caused by fever, exercise, dehydration, cold exposure, seizure, stress

**Orthostatic proteinuria**

**Glomerular diseases with isolated proteinuria:** Idiopathic (minimal change disease) nephrotic syndrome, focal segmental glomerulosclerosis, mesangial proliferative glomerulonephritis, membranous nephropathy, membranoproliferative glomerulonephritis, amyloidosis, diabetic nephropathy, sickle cell nephropathy

**Glomerular diseases with proteinuria as a prominent feature:** Acute postinfectious glomerulonephritis, immunoglobulin (Ig) A nephropathy

**Tubular disease:** Cystinosis, Wilson disease, acute tubular necrosis, tubulointerstitial nephritis, polycystic kidney disease, renal dysplasia

Data from Kliegman RM, Stanton BF, St. Geme JW, et al. *Nelson Textbook of Pediatrics*. 19th ed. Philadelphia: Saunders, 2011:1801.

## BOX 19-2

## BASIC EVALUATION OF SIGNIFICANT (NEPHROTIC AND NON-NEPHROTIC) PROTEINURIA

Complete metabolic panel with phosphorus  
C3 and C4

Antinuclear antibody, anti-double-stranded DNA

Hepatitis B, C, and HIV in high-risk populations

Antineutrophil antibodies (c- and p-ANCA)

Kidney and bladder ultrasonography

Referral to nephrologist

D. Evaluation<sup>16</sup>

Further evaluation is necessary if proteinuria is significant and not secondary to orthostatic proteinuria (Box 19-2).

E. Nephrotic Syndrome<sup>17</sup>

Manifestation of a glomerular disorder secondary to primary kidney disease, a systemic disorder resulting in glomerular injury, or rarely certain drugs

## 1. Clinical manifestations

Hypoalbuminemia and decrease in oncotic pressure results in generalized edema. Initial swelling commonly occurs on the face (especially periorbital), as well as in the pretibial area. Eye swelling is often mistaken for allergic reactions or seasonal allergies.

## 2. Etiologies (Table 19-8 and Box 19-3)

## 3. Management of minimal change nephrotic syndrome (MCNS): empirical corticosteroid treatment without kidney biopsy is recommended for children without atypical features. Hospitalization recommended for children with overwhelming edema or infection.

- a. Steroid-responsive: Roughly 95% of patients with MCNS and 20% with focal segmental glomerulosclerosis (FSGS) achieve remission within 4–8 weeks of starting prednisone. Prednisone starts with 60 mg/m<sup>2</sup> or 2 mg/kg/day (maximum dose, 60 mg/day) for 6 weeks, followed by

TABLE 19-8

ETIOLOGIES OF NEPHROTIC SYNDROME

Primary Causes (90%)	Secondary Causes (10%)
Minimal change nephrotic syndrome (MCNS): 85% of idiopathic causes in children	Infections (HIV, hepatitis B, hepatitis C)
Focal segmental glomerulosclerosis (FSGS)	Systemic lupus erythematosus
Membranous nephropathy	Diabetes mellitus
IgA nephropathy	Drugs
Genetic disorders involving the slit diaphragm	Malignancy (leukemias, lymphomas)

BOX 19-3

FACTORS SUGGESTING DIAGNOSIS OTHER THAN IDIOPATHIC MINIMAL CHANGE NEPHROTIC SYNDROME

- Age <1 year or >10 years
- Family history of kidney disease
- Extrarenal disease (arthritis, rash, anemia)
- Chronic disease of another organ or systemic disease
- Symptoms due to intravascular volume expansion (hypertension, pulmonary edema)
- Kidney failure
- Active urine sediment (red blood cell casts)

- 40 mg/m<sup>2</sup> or 1.5 mg/kg on alternate days for 6 weeks, followed by a prednisone taper. Response is the best prognostic indicator, including the likelihood of underlying MCNS.
- b. Frequently relapsing: Defined as two or more relapses within 6 months of initial response, or four or more relapses in any 12-month period.
  - c. Steroid-dependent: Defined as two consecutive relapses during tapering or within 14 days of cessation of steroids. Some patients can be managed with low-dose steroids given daily or on alternate days, but many still relapse. Second-line treatments for frequently relapsing and steroid-dependent nephrotic syndrome: Cyclophosphamide, mycophenolate mofetil (MMF), calcineurin inhibitors, or levamisole.
  - d. Steroid-resistant: Lack of remission or partial remission after 8 weeks of corticosteroids. Second-line agents, including calcineurin inhibitors or MMF, are often introduced once steroid resistance is confirmed.
  - e. Further evaluation: Biopsy recommended for macroscopic hematuria, persistent creatinine elevation, low complement levels, and persistent proteinuria after 4–8 weeks of adequate steroid treatment.
  - f. Complications: AKI, thromboembolic disease, infection, and side effects of systemic steroids.

VIII. TUBULAR DISORDERS

A. Renal Tubular Acidosis (Table 19-9)<sup>9,18</sup>

A group of transport defects resulting in abnormal urine acidification; due to deficiencies of reabsorption of bicarbonate (HCO<sub>3</sub><sup>-</sup>), excretion of

TABLE 19-9

## BIOCHEMICAL AND CLINICAL CHARACTERISTICS OF VARIOUS TYPES OF RENAL TUBULAR ACIDOSIS

	Type 1 (Distal)	Type 2 (Proximal)	Type 4 (Hypoaldosteronism)
Mechanism	Impaired distal acidification	Impaired bicarbonate absorption	Decreased aldosterone secretion or aldosterone effect
Etiology	Hereditary Sickle cell Toxins/drugs Cirrhosis Obstructive uropathy Connective tissue disorder	Hereditary Metabolic disease Fanconi syndrome Prematurity Toxins/heavy metals Amyloidosis PNH	Absolute mineralocorticoid deficiency Adrenal failure CAH DM Pseudohypoaldosteronism Interstitial nephritis
Minimal urine pH	>5.5	<5.5 (urine pH can be >5.5 with a bicarbonate load)	<5.5
Fractional excretion of bicarbonate (FeHCO <sub>3</sub> )	↓ (<5%)	↑ (>15%)	↓ (<5%)
Plasma K <sup>+</sup> concentration	Normal or ↓	Usually ↓	↑
Urine anion gap	Positive	Positive or negative	Positive
Nephrocalcinosis/nephrolithiasis	Common	Rare	Rare
Treatment	1–3 mEq/kg/day of HCO <sub>3</sub> (5–10 mEq/kg/day if bicarb wasting)	5–20 mEq/kg/day of HCO <sub>3</sub>	1–5 mEq/kg/day of HCO <sub>3</sub> May add Fludrocortisone and potassium binders

CAH, Congenital adrenal hyperplasia; DM, diabetes mellitus.; PNH, paroxysmal nocturnal hemoglobinuria.

Adapted from Holiday MA et al. *Pediatric Nephrology*. Baltimore: Williams & Wilkins, 1994:650.

hydrogen ions (H<sup>+</sup>), or both. Results in a persistent nonanion-gap metabolic acidosis accompanied by hyperchloremia. Renal tubular acidosis (RTA) syndromes often do not progress to kidney failure but are instead characterized by a normal GFR. Clinical presentation may be characterized by failure to thrive, polyuria, constipation, vomiting, and dehydration.

1. **Fractional excretion of bicarbonate (FeHCO<sub>3</sub>) should be checked after a HCO<sub>3</sub> load.** Can help differentiate the types of RTA. Equation is based on the same concept found in Section IV.B.1:

$$\text{FeHCO}_3 = ([\text{UHCO}_3]/\text{PHCO}_3)/[\text{UCr}/\text{PCr}] \times 100\%$$

2. **Urine anion gap (UAG) is useful in differentiating types of RTA,** but it should not be used when a patient is volume depleted or has an anion-gap metabolic acidosis.

$$\text{UAG} = \text{UNa} + \text{UK} - \text{UCI}$$

### B. Type 3 (Combined Proximal and Distal) RTA

Infants with mild type 1 and mild type 2 defects were previously classified as type 3 RTA. Studies have shown that this is not a genetic entity itself, which has resulted in reclassification as a subtype of type 1 RTA that occurs primarily in premature infants.

### C. Fanconi Syndrome

Generalized dysfunction of the proximal tubule resulting not only in bicarbonate loss but also in variable wasting of phosphate, glucose, and amino acids. May be hereditary, as in cystinosis and galactosemia, or acquired through toxin injury and other immunologic factors. Clinically characterized by rickets and impaired growth.

### D. Nephrogenic Diabetes Insipidus

1. **Water conservation is dependent on antidiuretic hormone (ADH) and its effects on the distal renal tubules.** Polyuria, a hallmark of nephrogenic diabetes insipidus (NDI), is due to diminished or lack of response of the ADH receptor in the distal renal tubules. Hereditary defects of ADH receptor or acquired insults (e.g., interstitial nephritis, sickle cell disease, lithium toxicity, chronic kidney disease [CKD]) may underlie NDI.
2. **Must be differentiated from other causes of polyuria:**
  - a. Central diabetes insipidus: ADH deficiency that may be idiopathic or acquired (through infection or pituitary trauma)
  - b. Diabetes mellitus
  - c. Psychogenic polydipsia
  - d. Cerebral salt wasting

## IX. CHRONIC KIDNEY DISEASE<sup>13</sup>

Kidney damage for >3 months, as defined by structural or functional abnormalities, with or without decreased GFR. Classified as:

Stage I: Kidney injury with normal or increased GFR

Stage II: GFR 60–89 mL/min/1.73 m<sup>2</sup>

Stage III: GFR 30–59 mL/min/1.73 m<sup>2</sup>

Stage IV: GFR 15–29 mL/min/1.73 m<sup>2</sup>

Stage V: GFR <15 mL/min/1.73 m<sup>2</sup> or dialysis

### A. Etiology

There is a close association with age when kidney failure is first detected. CKD in children <5 years is most commonly due to congenital abnormalities (e.g., kidney hypoplasia/dysplasia, urologic malformations), whereas older children more commonly have acquired glomerular diseases (e.g., glomerulonephritis, FSGS) or hereditary disorders (e.g., Alport syndrome).

### B. Clinical Manifestations (Table 19-10)

#### 1. Edema:

Secondary to excessive accumulation of both Na<sup>+</sup> and water. Causes of generalized edema include:

TABLE 19-10

## CLINICAL MANIFESTATIONS OF CHRONIC KIDNEY DISEASE

Manifestation	Mechanisms
Uremia	Decline in GFR
Acidosis	Urinary bicarbonate wasting Decreased excretion of $\text{NH}_4$ and acid
Sodium wasting	Solute diuresis, tubular damage Aldosterone resistance
Sodium retention	Nephrotic syndrome CHF Reduced GFR
Urinary concentrating defect	Solute diuresis, tubular damage ADH resistance
Hyperkalemia	Decline in GFR, acidosis Aldosterone resistance
Renal osteodystrophy	Impaired production of 1,25 (OH) vitamin D Decreased intestinal calcium absorption Impaired phosphorus excretion Secondary hyperparathyroidism
Growth retardation	Protein-calorie deficiency Renal osteodystrophy Acidosis Anemia Inhibitors of insulin-like growth factors
Anemia	Decreased erythropoietin production Low-grade hemolysis Bleeding, iron deficiency Decreased erythrocyte survival Inadequate folic acid intake Inhibitors of erythropoiesis
Bleeding tendency	Thrombocytopenia Defective platelet function
Infection	Defective granulocyte function Glomerular loss of immunoglobulin/opsonins
Neurologic complaints	Uremic factors
Gastrointestinal ulceration	Gastric acid hypersecretion/gastritis Reflux Decreased motility
Hypertension	Sodium and water overload Excessive renin production
Hypertriglyceridemia	Diminished plasma lipoprotein lipase activity
Pericarditis and cardiomyopathy	Unknown
Glucose intolerance	Tissue insulin resistance

ADH, Anti-diuretic hormone; CHF, congestive heart failure; GFR, glomerular filtration rate;  $\text{NH}_4$ , ammonium.

Adapted from Brenner BM. *Brenner and Rector's The Kidney*. 6th ed. Philadelphia: WB Saunders, 2000.



- a. Inability to excrete  $\text{Na}^+$  with or without water (e.g., glomerular diseases resulting in decreased GFR)
  - b. Decreased oncotic pressure (e.g., nephrotic syndrome, protein-losing enteropathy, hepatic failure, CHF)
  - c. Reduced cardiac output (e.g., CHF, pericardial disease)
  - d. Mineralcorticoid excess (e.g., hyperreninemia, hyperaldosteronism)
2. **Other manifestations below in Table 19-10**

## X. CHRONIC HYPERTENSION 20-22

**NOTE:** For management of acute hypertension and normal BP parameters, see Chapters 4 and 7.

### A. Definition

1. **Normal blood pressure (BP):** Systolic and diastolic BP <90th percentile for age, gender, and height. See Tables 7-1 and 7-2.
2. **High-normal BP (prehypertension):** Systolic and/or diastolic BP between 90th and 95th percentiles for age, gender, and height, or if BP exceeds 120/80 (even if <90th percentile for age, gender, and height).
3. **Hypertension:** Systolic and/or diastolic BPs >95th percentile for age, gender, and height on three separate occasions.
4. **Measurement of BP in children:**
  - a. Children  $\geq 3$  years should have BP measured at all routine and emergency visits. Children <3 years with risk factors (e.g., history of prematurity/low birth weight, congenital heart disease, kidney disease or family history of kidney disease, history of malignancy, solid organ or bone marrow transplant) should have BP measured.
  - b. BP should be measured in a seated position 5 minutes after resting quietly; auscultation is preferred.
  - c. Appropriate cuff size has a bladder width at least 40% of upper arm circumference at midway point. Bladder length should cover 80%–100% of arm circumference. Cuffs that are too small may result in falsely elevated BPs. Choose a larger-sized cuff if there is a choice between two.

### B. Etiologies of Hypertension in Neonates, Infants, and Children (Table 19-11)

### C. Evaluation of Chronic Hypertension

1. **Rule out factitious causes of hypertension** (improper cuff size or measurement technique [e.g., manual vs. oscillometric]), nonpathologic causes of hypertension (e.g., fever, pain, anxiety, muscle spasm), and iatrogenic mechanisms (e.g., medications, excessive fluid administration).
2. **History:** Headache, blurred vision, dyspnea on exertion, edema, obstructive sleep apnea (OSA) symptoms, endocrine symptoms (diaphoresis, flushing, constipation, weakness, etc.), history of neonatal intensive care unit (NICU) stay, rule out pregnancy, history of UTIs, history of medications and supplements, illicit drug use, or any family history of kidney dysfunction or hypertension.

TABLE 19-11

## CAUSES OF HYPERTENSION BY AGE GROUP

Age	Most Common	Less Common
Neonates/infants	Renal artery thrombosis after umbilical artery catheterization Coarctation of aorta Renal artery stenosis	Bronchopulmonary dysplasia Medications Patent ductus arteriosus Intraventricular hemorrhage
1–10 yr	Renal parenchymal disease Coarctation of aorta	Renal artery stenosis Hypercalcemia Neurofibromatosis Neurogenic tumors Pheochromocytoma Mineralocorticoid excess Hyperthyroidism Transient hypertension Immobilization-induced Sleep apnea Essential hypertension Medications
11 yr–adolescence	Renal parenchymal disease Essential hypertension	All diagnoses listed in this table

Modified from Sinaiiko A. Hypertension in children. *N Engl J Med*. 1996;335:26.

3. **Physical examination:** Four-extremity pulses and BPs, endocrine disease stigmata, edema, hypertrophied tonsils, skin lesions, abdominal mass, or abdominal bruit.
4. **Clinical evaluation of confirmed hypertension:**
  - a. Laboratory studies: UA with microscopic evaluation, urine culture, serum electrolytes, CBC, Cr, BUN, fasting glucose, and lipid panel.
  - b. Imaging: Kidney and bladder ultrasonography and echocardiography. Consider renovascular imaging as indicated.
  - c. Consider (as indicated) thyroid function tests, urine catecholamines, plasma and urinary steroids, plasma renin, aldosterone, and toxicology screen. Consider polysomnography and retinal examination.
5. **Consider referral to specialist in hypertension.**

#### D. Treatment of Hypertension

1. **Nonpharmacologic:** Aerobic exercise, sodium restriction, smoking cessation, and weight loss indicated in all patients with hypertension. Reevaluate BP after lifestyle interventions, and begin pharmacologic therapy if hypertension persists.
2. **Pharmacologic:** Indications include secondary hypertension, symptomatic hypertension, target-organ damage, diabetes mellitus, and persistent hypertension despite nonpharmacologic measures.

#### E. Classification of Hypertension in Children and Adolescents, with Measurement Frequency and Therapy Recommendations (Table 19-12)

**TABLE 19-12**  
**CLASSIFICATION OF HYPERTENSION IN CHILDREN AND ADOLESCENTS AND THERAPY RECOMMENDATIONS**

	SBP or DBP Percentile	Frequency of BP Measurement	Pharmacologic Therapy (in Addition to Lifestyle Modifications)
Normal	<90th percentile	Recheck at next physical examination	None
Prehypertension	90th to <95th percentile or if BP exceeds 120/80 mm Hg even if <90th percentile	Recheck in 6 months	None unless compelling indications: CKD, DM, heart failure, or LVH
Stage 1 hypertension	95th–99th percentile plus 5 mm Hg	Recheck in 1–2 weeks, sooner if patient is symptomatic; if persistently elevated on 2 additional occasions, evaluate or refer	Initiate therapy based on symptoms, secondary hypertension, end-organ damage, diabetes, persistent hypertension despite non-pharmacologic measures
Stage 2 hypertension	>99th percentile plus 5 mm Hg	Evaluate or refer within 1 week or immediately if the patient is symptomatic	Initiate therapy

CKD, Chronic kidney disease; DBP, diastolic blood pressure; DM, diabetes mellitus; LVH, left ventricular hypertrophy; SBP, systolic blood pressure.

Modified from National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents: The fourth report on the diagnosis, evaluation and treatment of high blood pressure in children and adolescents. *Pediatrics*. 2004;114:555-576.

F. Antihypertensive Drugs for Outpatient Management of Hypertension in Children 1–17 Years of Age (Table 19-13)

XI. NEPHROLITHIASIS 462A

A. Epidemiology

Lower incidence than adults but increasingly recognized.

B. Risk Factors

Congenital and structural urologic abnormalities (urinary stasis), hypercalciuria, hyperoxaluria/oxalosis, hypocitraturia, other metabolic abnormalities.

C. Presentation

Microscopic hematuria (90%), flank/abdominal pain (50%–75%), gross hematuria (30%–55%), concomitant UTI in up to 20%. Have higher likelihood than adults of having asymptomatic stones, especially younger children.

D. Diagnosis

Ultrasonography is an effective and preferred modality, particularly at centers with expertise, given benefit of avoiding radiation exposure. In certain scenarios (radiolucent stones such as uric acid stones, ureteral stones,

TABLE 19-13

**ANTIHYPERTENSIVE DRUGS FOR OUTPATIENT MANAGEMENT OF HYPERTENSION IN CHILDREN 1–17 YEARS OF AGE**

Class	Drug	Comments
Angiotensin-converting enzyme (ACE) inhibitor	Benazepril	Blocks angiotensin I to angiotensin II
	Captopril	Decreases proteinuria while preserving renal function
	Enalapril	
	Fosinopril	Contraindicated in pregnancy, compromised renal perfusion
	Lisinopril	
Angiotensin-II receptor blocker (ARB)	Quinapril	Check serum potassium and creatinine periodically to monitor for hyperkalemia and uremia Monitor for cough and angioedema
	Irbesartan	Contraindicated in pregnancy
$\alpha$ - and $\beta$ -Blockers	Losartan	Check serum potassium and creatinine periodically to monitor for hyperkalemia and uremia
	Labetalol	Causes decreased peripheral resistance and decreased heart rate
$\beta$ -Blocker	Carvedilol	Contraindications: asthma, heart failure, insulin-dependent diabetes Heart rate is dose-limiting May impair athletic performance
	Atenolol	Decreases heart rate, cardiac output, and renin release.
	Metoprolol	Noncardioselective agents (e.g., propranolol) are contraindicated in asthma and heart failure
	Propranolol	Metoprolol and atenolol are $\beta_1$ selective Heart rate is dose-limiting May impair athletic performance
		Should not be used in insulin-dependent diabetics
Calcium channel blocker	Amlodipine	Acts on vascular smooth muscles
	Felodipine	Renal perfusion/function is minimally affected; generally few side effects
	Isradipine	Amlodipine and isradipine can be compounded into suspensions
	Extended-release nifedipine	May cause tachycardia
Central $\alpha$ -agonist	Clonidine	Stimulates brainstem $\alpha_2$ receptors and decreases peripheral adrenergic drive May cause dry mouth and/or sedation ( $\downarrow$ opiate withdrawal) Transdermal preparation also available Sudden cessation of therapy can lead to severe rebound hypertension

TABLE 19-13

**ANTIHYPERTENSIVE DRUGS FOR OUTPATIENT MANAGEMENT OF HYPERTENSION IN CHILDREN 1–17 YEARS OF AGE (Continued)**

Class	Drug	Comments
Diuretic	Furosemide	Side effects are hyponatremia, hypokalemia, and ototoxicity
	Bumetanide	
	Hydrochlorothiazide (HCTZ)	Side effects are hypokalemia, hypercalcemia, hyperuricemia, and hyperlipidemia
	Chlorthalidone	
	Spironolactone	Useful as add-on therapy in patients being treated with drugs from other drug classes
Peripheral $\alpha$ -antagonist	Triamterene	Potassium-sparing diuretics are modest antihypertensives. They may cause severe hyperkalemia, especially if given with ACE inhibitor or ARB
	Amiloride	
Peripheral $\alpha$ -antagonist	Doxazosin	May cause hypotension and syncope, especially after first dose
	Prazosin	
	Terazosin	
Vasodilator	Hydralazine	Hydralazine can cause a lupus-like syndrome Directly acts on vascular smooth muscle and is very potent Tachycardia, Na retention, and water retention are common side effects
	Minoxidil	Used in combination with diuretics or $\beta$ -blockers Minoxidil is usually reserved for patients with hypertension resistant to multiple drugs

Modified from National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. *Pediatrics*. 2004;114:568-569; Hospital for Sick Children. *The HSC Handbook of Pediatrics*. 9th ed. St. Louis: Mosby, 1997; Sinaiko A. Treatment of hypertension in children. *Pediatr Nephrol*. 1994;8:603-609; and Khattak S et al. Efficacy of amlodipine in pediatric bone marrow transplant patients. *Clin Pediatr*. 1998;37:31-35.

and lack of ultrasonographic expertise), noncontrast helical CT may be preferred to improve diagnostic sensitivity.

### E. Management:

- 1. Pain control, urine culture, hydration.** Some centers initiate  $\alpha$ -blockers to facilitate stone passage, although evidence of benefit in children is equivocal.
- 2. Urologic intervention** (extracorporeal shock wave lithotripsy, ureteroscopy, and percutaneous nephrolithostomy). May be necessary in setting of unremitting pain or urinary obstruction, especially in the setting of AKI or at-risk patient (e.g., solitary kidney, etc.).
- 3. Collect and analyze stone composition to aid in prevention of future stones.**

### F. Workup

Up to 75% of children with a kidney stone will have a metabolic abnormality (e.g., hypercalciuria, hyperoxaluria, hyperuricosuria, cystinuria). Workup should include analysis of the stone (if possible), urinalysis, basic metabolic panel, and phosphate, magnesium, and uric acid levels.

If evidence of elevated calcium or phosphate, obtain parathyroid hormone (PTH) level and consider checking 25- and 1,25(OH) vitamin D levels. A 24-hour urine collection should be obtained several weeks after the stone has passed, and urine sodium, calcium, urate, oxalate, citrate, creatinine, and cystine should be evaluated.

## G. Prevention

1. **Recurrence of a kidney stone in children is common.**
2. **All children with history of stones should increase fluid intake** (e.g., at least 2 L/day in those >10 years old).
3. **Targeted interventions of any identified metabolic abnormalities** (e.g., low-sodium diet in those with hypercalciuria). Pharmacologic interventions are also available in certain scenarios (e.g., citrate supplementation).

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 See additional content on Expert Consult

### I. WEBSITES

Child Neurology Society: [www.childneurologysociety.org](http://www.childneurologysociety.org)

American Academy of Neurology Practice Guidelines: [aan.com/practice/guideline](http://aan.com/practice/guideline)

American Heart Association Statement on Management of Stroke in Infants and Children: [stroke.ahajournals.org](http://stroke.ahajournals.org)

### II. NEUROLOGIC EXAMINATION

#### A. Mental Status

Evaluate alertness and orientation to time, person, place, and current situation. Assess attentiveness and behavior in infants. Play interests are a window into development.

#### B. Cranial Nerves (Table 20-1)

#### C. Motor

1. **Muscle bulk.**
2. **Tone:** Infants with low tone will slip when held under their arms.
  - a. Passive movements: Resting resistance to examiner's movement
  - b. Active movements: Regulation of power with defined movements (e.g., posture, gait, pull to stand)
3. **Power/strength:** Assess and quantify activity (e.g., rising from floor, distance of standing broad jump, time to run 30 feet or climb 10 stairs [Box 20-1])

#### D. Sensory (Fig. 20-1, Table 20-2)

1. **Spinal cord level:** Best assessed with pinprick and temperature. If concerned about spinal cord impairment, ask about continence. Compare lower with upper, check both anterior and posterior trunk.
2. **Intraspinal lesions:**
  - a. Anterior pathways: Pinprick and temperature
  - b. Posterior pathways: Vibratory and joint position sense
3. **Root/plexus/nerve impairment:** Pin sensibility, consult dermatomal/nerve maps (see Fig. 20-1)
4. **Polyneuropathy:** Large fiber (vibration and position sense) versus small fiber (pinprick and temperature). Compare distal with proximal sites in a limb, and lower with upper extremities.

#### E. Tendon Reflexes

This assessment is most helpful in localizing other abnormalities, especially in the presence of weakness or asymmetry. Compare right with



**TABLE 20-1**  
**CRANIAL NERVES**

Function/Region	Cranial Nerve	Test/Observation
Olfactory	I	Smell (e.g., coffee, vanilla, peppermint)
Vision	II	Acuity, fields, fundus
Pupils	II, III	Sympathetics, size, reaction to light, accommodation
Eye movements and eyelids	III, IV, VI	Range and quality of eye movements, saccades, pursuits, nystagmus, ptosis
Sensation	V	Corneal reflexes, facial sensation
Muscles of mastication	V	Clench teeth
Facial strength	VII	Degree of expression of emotions; strength of eye closure, smile, and puffing out cheeks; facial symmetry
Hearing	VIII	Localize sound, attend to finger rub, audiologic testing
Mouth, pharynx	IX, X	Swallowing, speech quality, symmetrical palatal elevation, gag reflex
Head control	XI	Lateral head movement, shoulder shrug
Tongue movement	XII	Tongue protrusion

<b>BOX 20-1</b>
<b>STRENGTH RATING SCALE</b>
0/5: No movement (i.e., no palpable tension at tendon)
1/5: Flicker of movement
2/5: Movement in a gravity-neutral plane
3/5: Movement against gravity, but not resistance
4/5: Subnormal strength against resistance
5/5: Normal strength against resistance

left sides, upper with lower extremities, and distal with proximal reflexes (Box 20-2 and Table EC 20-A on Expert Consult).

1. **Isolated abnormality of reflexes:** Little significance in the setting of normal strength and coordination
2. **Brisk reflexes combined with weakness:** Indicate upper motor neuron disorder
3. **Absent reflexes:**
  - a. Muscle disease: Reflexes usually diminished commensurate with power
  - b. Selective reflex dropout: Spinal cord, root, or nerve lesion

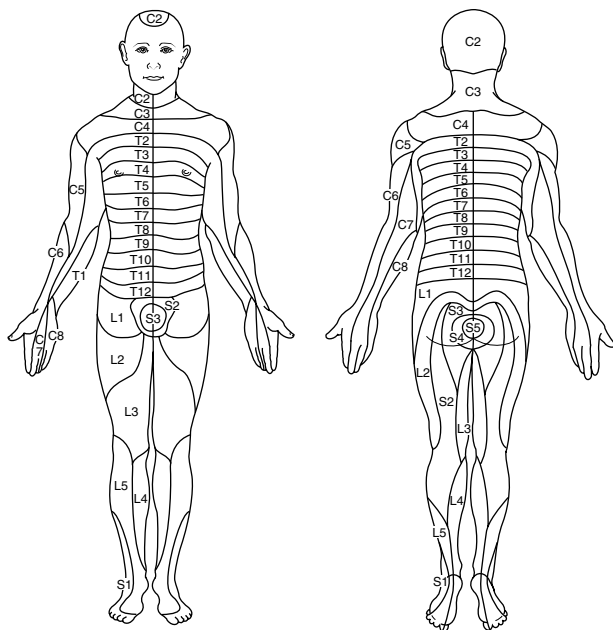
**F. Coordination and Movement**

1. **Evaluate general coordination while watching activities** (e.g., throwing a ball, dressing, writing, drawing)
2. **Test for cerebellar function:** Rapid alternating movements, finger-to-nose, heel-to-shin, walking, running
3. **Extra movements:** Quality and conditions under which they are enhanced or suppressed (tremor, dystonia, chorea, athetosis, tics, myoclonus)

TABLE EC 20-A

**MUSCLE STRETCH REFLEXES**

Reflex	Main Spinal Nerve Roots Involved
Biceps	C5, C6
Brachioradialis	C6
Triceps	C7
Knee	L4
Ankle	S1

**FIGURE 20-1**

Dermatomes. (From Athreya BH, Silverman BK. Pediatric physical diagnosis. Norwalk, CT: Appleton-Century-Crofts; 1985:238-239.)

**TABLE 20-2****UPPER AND LOWER MOTOR NEURON FINDINGS**

On Exam	Upper	Lower
Power	Decreased	Decreased
Reflexes	Increased	Decreased
Tone	Increased	Normal or decreased
Babinski	Upgoing (present)	Downgoing (normal)
Fasciculations	Absent	Present
Muscle wasting	Absent	Present

**BOX 20-2****REFLEX RATING SCALE**

- 0: None
- 1+: Diminished (need use of clasped hands/gritting teeth to engage reflex)
- 2+: Normal
- 3+: Increased (reflexes cross neighboring joint or cross to other side)
- 4+: Hyperactive with clonus

### III. HEADACHES -3

#### A. Evaluation of Headaches

1. **Classification:** Primary versus secondary<sup>4</sup>
  - a. Primary headaches: Migraines, tension-type, cluster, trigeminal autonomic cephalgias (TACs)
  - b. Secondary headaches: Caused by other underlying pathologies. Differential diagnoses in [Boxes 20-3 and 20-4](#).
2. **History and physical examination:** See [Boxes 20-5 and 20-6](#) and [Table EC 20-B on Expert Consult](#).
3. **Studies**<sup>2</sup>
  - a. Neuroimaging: Not indicated if there are no red flags on history and neurologic and funduscopic exams are normal. Computed tomography (CT [without contrast]) or magnetic resonance imaging (MRI) should be obtained for focal neurologic findings, suspected increased intracranial pressure, abnormal level of consciousness, atypical or progressive headaches, seizures, and abrupt-onset severe headache. CT provides poor imaging of the posterior fossa (see Chapter 25 for more detailed advantages of each modality).

#### BOX 20-3

##### DIFFERENTIAL DIAGNOSIS OF ACUTE HEADACHE

Evaluation of the first acute headache should exclude pathologic causes listed here before more common etiologies are considered.

1. Increased intracranial pressure (ICP): Trauma, hemorrhage, tumor, hydrocephalus, pseudotumor cerebri, abscess, arachnoid cyst, cerebral edema
2. Decreased ICP: After ventriculoperitoneal shunt, lumbar puncture, cerebrospinal fluid leak from basilar skull fracture
3. Meningeal inflammation: Meningitis, leukemia, subarachnoid or subdural hemorrhage
4. Vascular: Vasculitis, arteriovenous malformation, hypertension, cerebrovascular accident
5. Bone, soft tissue: Referred pain from scalp, eyes, ears, sinuses, nose, teeth, pharynx, cervical spine, temporomandibular joint
6. Infection: Systemic infection, encephalitis, sinusitis, etc.
7. First migraine

#### BOX 20-4

##### DIFFERENTIAL DIAGNOSIS OF RECURRENT OR CHRONIC HEADACHES

1. Migraine (with or without aura)
2. Tension
3. Analgesic rebound
4. Caffeine withdrawal
5. Sleep deprivation (e.g., in children with sleep apnea) or chronic hypoxia
6. Tumor
7. Psychogenic: conversion disorder, malingering, depression, acute stress, mood disorder
8. Cluster headache
9. Chronic daily headache

TABLE EC 20-B

**PHYSICAL AND NEUROLOGIC EXAMINATION OF THE CHILD WHO HAS HEADACHES<sup>2</sup>**

Feature	Significance
Growth parameters	Chronic illness may affect linear growth Hypothalamic-pituitary dysfunction may disturb growth
Head circumference	Increased intracranial pressure before fusion of sutures may accelerate head growth
Skin	Evidence of trauma or a neurocutaneous disorder
Blood pressure	Hypertension
Neurologic exam	Signs of increased intracranial pressure Focal abnormality
Cranial bruits	May reflect an intracranial arteriovenous malformation
Fundoscopic exam	Papilledema may reflect elevated intracranial pressure or pseudotumor cerebri

## BOX 20-5

**HEADACHE WARNING SIGNS ON HISTORY**

1. Pain that awakens child from sleep
2. Age <3 years
3. Pain made worse with straining or Valsalva
4. Explosive onset
5. Focal deficits
6. Headache associated with emesis
7. Changes in chronic pattern or steady worsening of headaches
8. Altered mental status: Changes in mood, personality, school performance
9. Concurrent fever

## BOX 20-6

**IMPORTANT HISTORICAL INFORMATION IN EVALUATING HEADACHE**

1. Age at onset
2. Associated trauma
3. Presence or absence of aura
4. Change in weight or other constitutional symptoms
5. Change in vision or any other neurologic symptoms
6. Frequency, severity, and duration of headaches (ask about school absences)
7. Quality, site, and radiation of pain (focal occipital pain is concerning for secondary headaches)
8. Associated symptoms such as weakness, tingling, photophobia, phonophobia
9. Triggers and alleviating/exacerbating factors
10. Family history of migraine
11. Changes and new stressors in school or at home

## BOX 20-7

**LUMBAR PUNCTURE<sup>5</sup>**

- Indications: Fever, infection, concern for pseudotumor cerebri or other causes of increased intracranial pressure after negative imaging.
- Contraindications: Elevated intracranial pressure or mass effect, owing to concern for herniation. Obtain a head CT before lumbar puncture if this is a concern.
- Standard tests: Cell counts + differential, Gram stain, cerebrospinal fluid (CSF) culture, protein, glucose. Consider viral studies (HSV, enterovirus, etc.).
- Special tests: Manometer for opening pressure if concern for pseudotumor cerebri. Performed in a lateral decubitus position with legs extended.
- Correction for white blood cells (WBCs): Expected CSF WBC count = (red blood cells [RBCs] CSF/RBCs serum) × WBCs serum.
- Xanthochromia: Yellow or pink discoloration of CSF due to breakdown of hemoglobin. If CSF is xanthochromic, suspect subarachnoid hemorrhage.

- b. Laboratory studies: Not routinely indicated if no red flags
- c. Lumbar puncture: Not routinely indicated if no red flags (Box 20-7)
- d. Electroencephalogram (EEG): Not routinely indicated if no red flags

**B. Migraine Headache**

1. Box 20-8 lists diagnostic criteria. Migraines are typically throbbing, pulsatile, or pressure-like in children. They are usually bifrontal in children

## BOX 20-8

**DIAGNOSTIC CRITERIA FOR PEDIATRIC MIGRAINE WITHOUT AURA<sup>4,6</sup>**

At least five attacks fulfilling the following criteria and not attributable to another disorder:

1. Headache lasts 1–72 hours (untreated or unsuccessfully treated)
2. At least two of the following characteristics:
  - a. Unilateral or bilateral
  - b. Pulsating quality
  - c. Moderate to severe in intensity
  - d. Aggravated by or causing avoidance of routine physical activities
3. At least one of the following occur during the headache:
  - a. Nausea and/or vomiting
  - b. Photophobia and phonophobia (which may be inferred from behavior)

and unilateral in adolescents and adults. There are many potential triggers (e.g., stress, caffeine, menses, sleep disruption).

2. **Classification<sup>4</sup>:**

- a. Classic: With aura. *Aura* is any neurologic symptom that occurs prior to onset of a migraine (e.g., visual aberrations, paresthesias, numbness, dysphasia).
- b. Common: Without aura
3. **Precursors to migraines and close associations include** cyclic vomiting, abdominal migraines, recurrent abdominal pain, paroxysmal vertigo of childhood, paroxysmal torticollis of infancy, and motion sickness.
4. **Treatment<sup>7,8</sup>:** Includes reassurance and education regarding lifestyle modification (sleep, hygiene, exercise, stress reduction, fluids, not missing meals). Refer any child with focal neurologic deficits to a pediatric neurologist.
  - a. Acute symptomatic: Avoid medication overuse (>2-3 doses/week); it can lead to rebound headache.
    - (1) Dark, quiet room and sleep.
    - (2) Nonsteroidal antiinflammatory drugs (NSAIDs [e.g., naproxen, ibuprofen, ketorolac]).
    - (3) Acetaminophen.
    - (4) Caffeine (e.g., Excedrin).
    - (5) Triptans (Table 20-3). Objective data support nasal sumatriptan, which has been studied in children as young as 5 years of age. In 2009, the U.S. Food and Drug Administration (FDA) approved almotriptan for migraine treatment in adolescents aged 12–17.
    - (6) Antiemetics (e.g., metoclopramide, prochlorperazine, promethazine) if nausea is a factor.
    - (7) Steroids (e.g., methylprednisolone) may be useful in intractable cases, although evidence is lacking.
    - (8) Magnesium may be useful in intractable cases, although evidence is lacking.
    - (9) Sodium valproate.

TABLE 20-3

**ABORTIVE TRIPTANS FOR MIGRAINE (SEE FORMULARY FOR SPECIFIC DOSING)**

Medication	Dose (Preparation*)	Duration†
Sumatriptan (Imitrex)	6 mg (SQ); 5, 20 mg (NS); 25, 50, 100 mg (T)	Short
Rizatriptan (Maxalt)	5, 10 mg (T); 5, 10 mg (D)	Short
Zolmitriptan (Zomig)	2.5, 5 mg (T); 2.5, 5 mg (D); 5 mg (NS)	Short
Almotriptan (Axert)	6.25, 12.5 mg (T)	Short
Eletriptan (Relpax)	20, 40 mg (T)	Short
Naratriptan (Amerge)	1, 2.5 mg (T)	Long
Frovatriptan (Frova)	2.5 mg (T)	Long

\*D, Dissolvable tablet; NS, nasal spray; SQ, subcutaneous; T, tablet.

†Short (4-hr half-life); long (12- to 24-hr half-life).

TABLE 20-4

**PREVENTIVE THERAPIES FOR MIGRAINE (SEE FORMULARY FOR DOSING)**

Medications	Adverse Effects	Consider in Patients with the Following Comorbidities
<b>ANTICONVULSANT MEDICATIONS</b>		
Divalproex sodium (Depakote)	Dizziness, drowsiness, weight gain, gastrointestinal upset, teratogenicity, potential liver injury	Bipolar, epilepsy, underweight
Topiramate (Topamax)	Cognitive changes, weight loss, sensory changes, paresthesias, kidney stones	Obesity, epilepsy
<b>ANTIDEPRESSANT MEDICATIONS</b>		
Amitriptyline (Elavil)	Sedation, dry mouth, constipation	Depression, insomnia
Nortriptyline	Sedation, dry mouth, constipation	Depression, insomnia
<b>ANTIHISTAMINE MEDICATION</b>		
Cyproheptadine (Periactin)	Sedation, increased appetite	Seasonal allergies, poor appetite, insomnia
<b>β-BLOCKER</b>		
Propranolol (Inderal)	Hypotension, exacerbates exercise-induced asthma, masks hypoglycemia	Hypertension
<b>CALCIUM CHANNEL BLOCKER</b>		
Flunarizine	Drowsiness, weight gain	Hypertension

b. Chronic treatment (if >3 per month and if migraines interfere with daily functioning or school):

- (1) Avoid triggers and stress. Balanced diet restrictive of certain migraine-causing foods (especially caffeine). Headache journal to help identify potential triggers. Encourage aerobic exercise and regular sleep. Keep hydrated.
- (2) Offer counseling when appropriate; also consider biofeedback, acupuncture, yoga, and massage therapy if parents are interested.
- (3) Consider medications (Table 20-4)



IV. PAROXYSMAL EVENTS

A. Differential Diagnosis of Recurrent Events That Mimic Epilepsy in Childhood (Table 20-5)

B. Seizures: First and Recurrent<sup>9,10</sup>

- 1. **Seizure:** Paroxysmal synchronized discharge of cortical neurons resulting in alteration of function (motor, sensory, cognitive)
- 2. **Causes of seizures**
  - a. Diffuse brain dysfunction: Fever, metabolic compromise, toxin or drugs, hypertension

TABLE 20-5  
DIFFERENTIAL DIAGNOSIS OF RECURRENT EVENTS THAT MIMIC EPILEPSY IN CHILDHOOD<sup>9</sup>

Event	Differentiation from Epilepsy
Pseudoseizure (psychogenic seizure)	No EEG changes except movement artifact during event; movements thrashing rather than clonic; brief/absent postictal period; most likely to occur in patient with epilepsy
Paroxysmal vertigo (toddler)	Patient frightened and crying; no loss of awareness; staggers and falls, vomiting, dysarthria
GER in infancy, childhood	Paroxysmal dystonic posturing associated with meals (Sandifer syndrome)
Breath-holding spells (18 mo–3 yr)	Loss of consciousness and generalized convulsions, always provoked by an event that makes child cry
Syncope	Loss of consciousness with onset of dizziness and clouded or tunnel vision; slow collapse to floor; triggered by postural change, heat, emotion, etc.
Cardiogenic syncope	Abnormal ECG/Holter monitor finding (e.g., prolonged QT, atrioventricular block, other arrhythmias); exercise a possible trigger; episodic loss of consciousness without consistent convulsive movement
Cough syncope	Prolonged cough spasm during sleep in asthmatic, leading to loss of consciousness, often with urinary incontinence
Paroxysmal dyskinesias	May be precipitated by sudden movement or startle; not accompanied by change in alertness
Shuddering attacks	Brief shivering spells with continued awareness
Night terrors (4–6 yr)	Brief nocturnal episodes of terror without typical convulsive movements
Rages (6–12 yr)	Provoked and goal-directed anger
Tics/habit spasms	Involuntary, nonrhythmic, repetitive movements not associated with impaired consciousness; suppressible
Narcolepsy	Sudden loss of tone secondary to cataplexy; emotional trigger; no postictal state or loss of consciousness; EEG with recurrent REM sleep attacks
Migraine (confusional)	Headache or visual changes that may precede attack; family history of migraine; autonomic or sensory changes that can mimic focal seizure; EEG with regional area of slowing during attack
Myoclonus	Involuntary muscle jerking or twitch

ECG, Electrocardiography; EEG, electroencephalography; GER, gastroesophageal reflux; REM, rapid eye movement.

- b. Focal brain dysfunction: Stroke, neoplasm, focal cortical dysgenesis, trauma
- 3. **Febrile illness**—associated seizures<sup>11</sup>
  - a. Definitions:
    - (1) Simple febrile seizure: Primary generalized seizure associated with fever in a child 6–60 months of age that is non-focal, lasts <15 minutes and does not recur in a 24-hour period
    - (2) Complex febrile seizure: Seizure associated with a fever in a child 6–60 months of age that is focal, lasts >15 minutes, or recurs within a 24-hour period
  - b. No further workup is necessary for a simple febrile seizure in a neurologically intact child who appears well, has a normal neurologic exam, is fully immunized, and has no meningeal signs.
  - c. Neuroimaging, blood work, and EEG are not routinely recommended in previously healthy children who have a simple febrile seizure. Further studies should be directed toward ascertaining the source of the fever.
  - d. Perform a lumbar puncture in any child with seizures and meningeal signs or symptoms (e.g., nuchal rigidity, Kernig and/or Brudzinski signs, etc.).
  - e. Consider lumbar puncture in these circumstances:
    - (1) Infant 6–12 months of age if incomplete or unknown *Haemophilus influenzae* or *Streptococcus pneumoniae* immunizations.
    - (2) Febrile seizure in a child pretreated with antibiotics. Antibiotics can mask signs and symptoms of meningitis.
- 4. **Evaluation of nonfebrile seizures**
  - a. If clinically indicated, check glucose, Na, K, Ca, Phos, blood urea nitrogen (BUN), creatinine (Cr), complete blood cell count (CBC), tox screen.
  - b. Blood pressure (BP): Supine and upright.
  - c. EEG: Recommended in all children with first nonfebrile seizure to evaluate for an epilepsy syndrome.<sup>12</sup> Routine interictal EEGs are frequently normal. Repeat EEGs, prolonged EEG monitoring with video, or studies done with sleep deprivation or photic stimulation may be more informative.
  - d. If this is not the first seizure and patient is receiving antiepileptic therapy, a change in seizure pattern should prompt a drug level (see [Table 20-7](#) for therapeutic drug levels).
  - e. Imaging: Although not required for diagnosis, MRI and CT can detect focal brain abnormalities that may predispose to focal seizures.
    - (1) Head ultrasound may be used in early infancy and requires open fontanelles.
    - (2) Head CT without contrast: Can detect mass lesions, acute hemorrhage, hydrocephalus, and calcifications secondary to congenital disease such as cytomegalovirus infection. Obtain a head CT only when concerned about a mass or bleed or in an emergency situation.
    - (3) Brain MRI with contrast: Obtain in infants with epilepsy and children with recurrent partial seizures, focal neurologic deficits, or developmental delay. Not routinely indicated when evaluating a first-time seizure.
- 5. **Seizure disorders (epilepsy):** Assess seizure type ([Table 20-6](#)), epilepsy classification ([Box 20-9](#)), and severity of disorder

TABLE 20-6

SPECIAL SEIZURE SYNDROMES<sup>9,13,14</sup>

Syndrome	Etiology	Evaluation	Treatment	Comment
Neonatal seizures	Brain malformation, hypoxic-ischemic encephalopathy, intracranial hemorrhage, inborn errors of metabolism, CNS infection, cerebral infarction, hypoglycemia, hypocalcemia, hypomagnesemia	Screen for electrolyte and metabolic abnormalities and pyridoxine deficiency, workup for sepsis, LP, head ultrasound, CT or MRI, EEG	Treat underlying abnormality, consider pyridoxine ± EEG, phenobarbital (± additional agents).	Occurs within first 28 days of life; may be myoclonic, tonic, clonic, or subtle; presents as blinking, chewing, bicycling, or apnea; distinguished from jitteriness by vital sign changes and inability to provoke or inhibit
Infantile spasms	Symptomatic—67%. May be secondary to CNS malformation, acquired infantile brain injury, tuberous sclerosis, inborn errors of metabolism Cryptogenic—33%	EEG (shows hypsarrhythmia), MRI	High-dose steroids, vigabatrin, topiramate, ketogenic diet	Usual onset after age 2 mo, peak onset 4–6 mo; initiate treatment as soon as possible. Presents as sudden flexion or extension of the trunk and extremities, often in clusters
Absence seizures	Unknown	EEG (sudden generalized 3-Hz spike and slow-wave discharges)	Ethosuximide, valproic acid	Age of onset 4–8 years; provoked by hyperventilation; staring spells ± automatisms (eye blinking, mouth movements); often resolves spontaneously by puberty; good neurologic outcome
Benign rolandic epilepsy/BECS (benign epilepsy of childhood with centrotemporal spikes)	Unknown	EEG (characteristic pattern of centrotemporal spikes)	No treatment necessary; avoid sleep deprivation; if seizures are frequent, may use carbamazepine or levetiracetam.	Age of onset 2–13 years; seizures are nocturnal and consist of hemisensory or motor phenomena of the face, motor findings in limbs; most patients outgrow by age 16–18.

Juvenile myoclonic epilepsy	Unknown genetic predisposition	Clinical history, sleep-deprived EEG (reveals generalized spike and wave discharges with normal background activity)	Levetiracetam, other meds for generalized seizure	Adolescent onset; morning myoclonus; 75%–95% have GTC seizures; good intellectual outcome, no progressive deterioration
Panayiotopoulos syndrome	Benign age-related focal seizure disorder Prolonged seizure with predominately autonomic symptoms	EEG (shifting and/or multiple foci, often occipital spikes)	Often not treated owing to benign nature of condition	Syndrome specific to childhood; symptoms include vomiting, pallor, eye deviation, sweating, $\pm$ convulsions
Lennox-Gastaut syndrome	Cryptogenic or symptomatic	Interictal EEG (reveals slow spike and wave discharges)	Pharmacologic and nonpharmacologic treatments have varying degrees of effectiveness.	Age of onset 1–8 years; multiple seizure types, often intractable; intellectual disability

CNS, Central nervous system; CT, computed tomography; EEG, electroencephalography; GTC, generalized tonic-clonic; LP, lumbar puncture; MRI, magnetic resonance imaging.

## BOX 20-9

INTERNATIONAL CLASSIFICATION OF EPILEPTIC SEIZURES<sup>10</sup>

- I. Partial seizures (seizures with focal onset)
  - 1. Simple partial seizures (consciousness unimpaired)
    - a. With motor signs
    - b. With somatosensory or special sensory symptoms
    - c. With autonomic symptoms or signs
    - d. With psychic symptoms (higher cerebral functions)
  - 2. Complex partial seizures (consciousness impaired)
    - a. Starting as simple partial seizures
      - (a) Without automatisms
      - (b) With automatisms (e.g., lip smacking, drooling, dazed-eyes look)
    - b. With impairment of consciousness at onset
      - (a) Without automatisms
      - (b) With automatisms
  - 3. Partial seizures evolving into secondarily generalized seizures
- II. Generalized seizures
  - 1. Absence seizures: Brief lapse in awareness without postictal impairment (atypical absence seizures may have mild clonic, atonic, tonic, automatism, or autonomic components)
  - 2. Myoclonic seizures: Brief, repetitive, symmetric muscle contractions
  - 3. Clonic seizures: Rhythmic jerking, flexor spasm of extremities
  - 4. Tonic seizures: Sustained muscle contraction
  - 5. Tonic-clonic seizures
  - 6. Atonic seizures: Abrupt loss of muscle tone
- III. Unclassified epileptic seizures

6. **Status epilepticus**<sup>15</sup>: Traditionally defined as continuous or recurrent seizures lasting  $\geq 30$  minutes without the patient regaining consciousness. For treatment purposes, status epilepticus can be diagnosed after 5 minutes of continuous seizure or at least two discrete seizures without complete recovery of consciousness between them. See Chapter 1 for treatment guidelines.

7. **Treatment**<sup>12,16</sup>:

- a. If patient's first seizure, seizure was nonfocal, and patient has returned to baseline: No antiepileptic medication indicated. Overall recurrence of seizure varies from 14%–65% in the first year. Most recurrences occur within 1–2 years after the initial event. Epileptiform abnormalities on EEG indicate a higher chance of recurrence.
- b. Educate parents and patient (as age appropriate) regarding epilepsy basics.<sup>17</sup> Review seizure first aid. Recommend supervision during bathing or swimming. Know driver's license laws in the state. Advocate teacher and school awareness.
- c. Pharmacotherapy (Table 20-7): Weigh risk of future seizures without therapy against risk for treatment side effects plus residual seizures despite therapy. Reserve pharmacotherapy for recurrent afebrile seizures. Monotherapy may reduce complications; polytherapy increases risk of complications and side effects more than efficacy.

TABLE 20-7

## COMMONLY USED ANTICONVULSANTS

Anticonvulsant (Trade Name)	Standard Therapeutic Levels (mg/dL)	Efficacy (Generalized/ Partial)	IV Preparation Available?	Side Effects
Carbamazepine (Tegretol/ Carbatrol)	8–12	P	No	Sedation, ataxia, diplopia, Stevens-Johnson syndrome, blood dyscrasias, hepatotoxicity, may worsen generalized seizures
Clobazam (Onfi)	n/a	G/P	No	Sedation, dizziness
Clonazepam (Klonopin)	n/a	G/P	No	Sedation, drooling, dependence
Ethosuximide (Zarontin)	40–100	G (absence)	No	Gastrointestinal upset
Felbamate (Felbatol)	40–100	G/P	No	Weight loss, hepatotoxicity, sleep disturbances, aplastic anemia (1:7900)
Gabapentin (Neurontin)	3–18	P	No	Weight gain, leg edema, dizziness
Lacosamide (Vimpat)	n/a	P	Yes	Sedation, reduced benefit with sodium channel drugs
Lamotrigine (Lamictal)	3–18	G/P	No	Rash (increased risk in combination with valproate)
Levetiracetam (Keppra)	30–60	G/P	Yes	Behavioral changes, irritability, rare psychosis
Oxcarbazepine (Trileptal)	MHD level (5–40)	P	No	Hyponatremia
Phenobarbital (Luminal)	15–40	G/P	Yes	Altered cognition, sedation
Phenytoin (Dilantin)	10–20	P	Yes	Hirsutism, gingival hyperplasia, teratogenicity, rash, purple-glove syndrome with infusion
Pregabalin (Lyrica)	n/a	P	No	Peripheral edema, weight gain, constipation, dizziness, ataxia, sedation
Rufinamide (Banzel)	n/a	G (Lennox-Gastaut)	No	Shortened QT interval, nausea, dizziness, sedation, headache
Tiagabine (Gabitril)	n/a	P	No	Can worsen generalized seizures
Topiramate (Topamax)	2–20	G/P	No	Cognitive side effects, weight loss, renal stones, acidosis, glaucoma
Valproic acid (Depakote, Depakene)	75–100	G/P	Yes	Weight gain, alopecia, hepatotoxicity, pancreatitis, PCOS, teratogenicity
Vigabatrin (Sabril)	n/a	G (infantile spasms)	No	Rash, weight gain, irritability, dizziness, sedation, visual field defects (requires ophthalmology evaluations)
Zonisamide (Zonegran)	20–40	G/P	No	Renal stones, weight loss; rare: Stevens-Johnson syndrome, aplastic anemia

G, Generalized; MHD, 10-Monohydroxy metabolite; n/a, not available; P, partial; PCOS, polycystic ovarian syndrome.

Based on personal communication with Eric Kossoff, MD, Johns Hopkins Pediatric Neurology.

- d. Ketogenic diet<sup>18</sup>: High-fat, low-carbohydrate therapy typically used for intractable seizures. Especially effective for infantile spasms, GLUT1 deficiency, Doose syndrome, pyruvate dehydrogenase deficiency. Urine ketones can be monitored to assess compliance. Side effects include acidosis with bicarbonate value as low as 10–15 mEq/L, kidney stones, growth disturbance, and constipation. Typically used for 2 years, but can be maintained for longer.

### C. Special Seizure Syndromes<sup>13,17</sup>

See Table 20-6 for seizure types, etiologies, evaluation, and treatment of many common seizure syndromes.

## V. HYDROCEPHALUS<sup>18</sup>

### A. Diagnosis<sup>19</sup>

Assess increasing head circumference, misshapen skull, frontal bossing, bulging large anterior fontanelle, increased ICP (setting-sun eye sign due to upward gaze paresis, increased tone/reflexes, vomiting, irritability, papilledema), and developmental delay. Obtain neuroimaging if increase in head circumference crosses more than two percentile lines or if patient is symptomatic. Differentiate hydrocephalus from megalencephaly or hydrocephalus *ex vacuo*.

### B. Treatment

#### 1. Medical:

- a. Emergently manage acute increase of ICP (see Chapter 4).  
b. Slowly progressive hydrocephalus: Acetazolamide and furosemide may provide temporary relief by decreasing the rate of CSF production (see Formulary for dosing).

#### 2. Surgical: CSF shunting

- a. Shunts: Ventriculoperitoneal (VP) shunts used most commonly.  
(1) Shunt dysfunction may be caused by infection, obstruction (clogging or kinking), disconnection, and migration of proximal and distal tips. Patient will develop signs of increased ICP with shunt malfunction.  
(2) Evaluation of shunt integrity: Obtain head CT to evaluate shunt position, ventricular size, and evidence of increased ICP. Obtain shunt series (skull, neck, chest, and abdominal radiographs) to look for kinking or disconnection. Referral to a neurosurgeon is then warranted to test shunt function and for possible percutaneous shunt drainage.  
b. Endoscopic third ventriculostomy (ETV) may be used to avoid ventricular shunting.

## VI. ATAXIA<sup>20,21</sup>

**A. Ataxia definition:** impaired coordination of movement and balance

### B. Differential Diagnosis of Acute Ataxia (Box 20-10)

### C. Evaluation (Box 20-11)

**BOX 20-10****DIFFERENTIAL DIAGNOSIS OF ACUTE ATAXIA**

1. Drug ingestion (e.g., phenytoin, carbamazepine, sedatives, hypnotics, phencyclidine) or intoxication (e.g., alcohol, ethylene glycol, hydrocarbon fumes, lead, mercury, thallium)
2. Postinfectious (cerebellitis [e.g., varicella], acute disseminated encephalomyelitis)
3. Head trauma (cerebellar contusion or hemorrhage, posterior fossa hematoma, vertebrobasilar dissection, postconcussive syndrome)
4. Basilar migraine
5. Benign paroxysmal vertigo (migraine equivalent)
6. Intracranial mass lesion (tumor, abscess, vascular malformation)
7. Opsoclonus-myoclonus: Chaotic eye movement combined with ataxia and myoclonus of either postinfectious or paraneoplastic (neuroblastoma or other neural crest tumors) etiology
8. Hydrocephalus
9. Infection (e.g., labyrinthitis)
10. Seizure (ictal or postictal)
11. Vascular events (e.g., cerebellar hemorrhage or stroke)
12. Guillain-Barré syndrome or Miller-Fisher variant (ataxia, ophthalmoplegia, and areflexia). Warning: If bulbar signs present, patient may lose ability to protect airway.
13. Rare inherited paroxysmal ataxias
14. Inborn errors of metabolism (e.g., mitochondrial disorders, aminoacidopathies, urea cycle defects) (See Chapter 13 for workup.)
15. Multiple sclerosis
16. Somatoform disorders (conversion)

**BOX 20-11****EVALUATION OF ACUTE ATAXIA (BASED ON CLINICAL SCENARIO)**

1. Complete blood cell count (CBC), electrolytes, urine and serum toxicology
2. Imaging (computed tomography [CT] and/or magnetic resonance imaging [MRI])
3. Lumbar puncture (LP)
4. Electroencephalography (EEG)
5. If neuroblastoma is suspected (opsoclonus-myoclonus), obtain urine vanillylmandelic acid and homovanillic acid and imaging of chest and abdomen.

**VII. STROKE 22-25****A. Etiology**

Risk factors for childhood stroke: Congenital heart disease, cerebral arteriopathies, hematologic disorders (sickle cell disease, prothrombotic state), serious systemic infection (meningitis, sepsis), head or neck trauma causing arterial dissection, and drugs



**BOX 20-12****DIFFERENTIAL DIAGNOSIS OF ACUTE-ONSET FOCAL NEUROLOGIC DEFICIT**

1. Hemiplegic migraine
2. Focal seizure
3. Postictal (Todd) paralysis
4. Cervical spinal cord injury (deficits spare face)
5. Ischemic stroke
6. Hemorrhagic stroke

**BOX 20-13****INITIAL WORKUP OF ACUTE STROKE**

1. Imaging: STAT noncontrast head computed tomography. Subsequently can obtain magnetic resonance imaging (diffusion-weighted) and magnetic resonance angiography of head and neck.
2. Initial laboratory studies: Complete blood cell count, comprehensive metabolic panel, erythrocyte sedimentation rate, prothrombin time, partial thromboplastin time, international normalized ratio, type and screen, urine toxicology screen
3. Echocardiogram
4. Hypercoagulability workup
5. Other studies to consider on a case-by-case basis: Fasting lipid panel, rheumatologic and metabolic studies, hemoglobin electrophoresis, and HIV testing

**B. Differential Diagnosis (Box 20-12)**

Stroke should be considered in the differential diagnosis for any child who presents with acute-onset focal neurologic deficit, focal seizures with prolonged postictal paralysis, new-onset refractory focal status epilepticus, altered mental status, or unexplained encephalopathy.

**C. Initial Workup (Box 20-13)****D. Management<sup>24</sup>**

1. **Supportive care is critical** and should proceed rapidly and parallel with initial workup. Ensure airway patency, provide supplemental oxygen to maintain  $\text{Sao}_2 > 94\%$ , and start maintenance intravenous (IV) fluids.
2. **Optimize cerebral perfusion pressure:** Ensure adequate fluid volume and maintenance of median BP for age. Treatment of hypertension is controversial. Unless BP is extremely elevated, *do not* use acute antihypertensive therapy, because hypertension may be a compensatory reaction to maintain cerebral perfusion.
3. **Monitoring:** Assess neurologic status frequently. Aim for normoglycemia (blood glucose 60–120 mg/dL). Treat fevers, with goal core temperature  $<37^\circ\text{C}$ . Treat seizures aggressively. Correct dehydration and anemia.
4. **Deep venous thrombosis (DVT) prophylaxis for immobilized patients.**
5. **Antiplatelet and anticoagulation therapy:** If no evidence of hemorrhage, aspirin is typically recommended (1–5 mg/kg/day). Long-term anticoagulation with low-molecular-weight heparin or warfarin may be considered by a specialist on a case-by-case basis in children with substantial risk

of recurrent cardiac embolism and cerebral venous sinus thrombosis, and in selected hypercoagulable states.

6. **Children with sickle cell disease:** Hydration and urgent exchange transfusion to reduce sickle hemoglobin to <30% is recommended. Consult hematology.
7. **Urgent neurology consultation,** along with transfer to a tertiary care center with expertise in childhood stroke.
8. **Thrombolytic therapy not recommended for children** (American Heart Association [AHA] guidelines).


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## Nutrition and Growth

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 See additional content on Expert Consult

### I. WEBSITES

#### A. Professional and Government Organizations:

1. Growth Charts and Nutrition Information: <http://www.cdc.gov>
2. AAP Children's Health Topics: <http://www.healthychildren.org>
3. Academy of Nutrition and Dietetics: <http://www.eatright.org>
4. American Society for Parenteral and Enteral Nutrition: <http://www.clinnutr.org>
5. National Institute of Child Health and Human Development: Breastfeeding: <http://www.nichd.nih.gov/health/topics/breastfeeding.cfm>
6. U.S. Department of Agriculture healthy eating guidelines: <http://www.cnpp.usda.gov/dietaryguidelines.htm> and <http://www.choosemyplate.gov>

#### B. Infant and Pediatric Formula Company Websites for Obtaining Complete and Up-to-Date Product Information. Information regarding more specialized and metabolic formulas can be found using these websites:

1. Enfamil, Enfacare, Nutramigen, and Pregestimil: <http://www.meadjohnson.com>
2. Carnation, Good Start, Nutren, Peptamen, Vivonex, Boost, and Resource: <http://www.nestle-nutrition.com> and <http://www.nestleinfantnutrition.com>
3. Alimentum, Elecare, Ensure, Neosure, Pediasure, Pedialyte, and Similac: <http://www.abbottnutrition.com>
4. America's Store Brand and Bright Beginnings: <http://www.pbmproducts.com>
5. Ketocal, Neocate, and Pepdite: <http://www.shsna.com>

### II. ASSESSMENT OF NUTRITIONAL STATUS

#### A. Elements of Nutritional Assessment

1. **Anthropometric measurements** (weight, length/height, head circumference, body mass index [BMI], skin folds): Data plotted on growth charts according to age and compared with a reference population
2. **Clinical assessment** (general appearance [e.g., hair, skin, oral mucosa] and gastrointestinal symptoms of nutritional deficiencies)
3. **Dietary evaluation** (feeding history, current intake)
4. **Physical activity and exercise**
5. **Laboratory findings** (comparison with age-based norms)

## B. Indicators of Nutritional Status<sup>1</sup> (Growth Charts) (Figs. 21-1 to 21-9; Figures EC 21-A to 21-G on Expert Consult)

1. **Growth:** Ideally, should be evaluated over time, but one measurement can be used for screening. Height (or length), weight, and weight for height should be plotted on a growth chart for every patient.
2. **BMI:** Defined as an index of healthy weight and a predictor of morbidity and mortality risk. Used to classify underweight and overweight individuals.<sup>2</sup> BMI should be determined and plotted for children  $\geq 2$  years. Use this formula to calculate BMI:

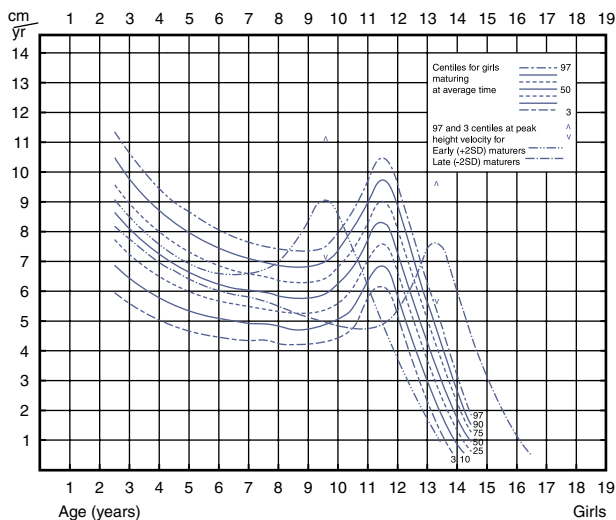
$$\text{BMI} = \text{wt (kg)} / [\text{height (m)}^2]$$

or

$$\text{BMI} = \text{wt (lb)} / [\text{height (in)}^2] \times 703$$

**NOTE:** Height indicates height measured by stadiometer, not recumbent length.

3. **BMI percentile:** BMI percentile is plotted on the Centers for Disease Control and Prevention (CDC) growth charts for children  $\geq 2$  years. Although not a direct measure of body fat, it is a reliable indicator of body fatness in most children and adolescents<sup>2</sup>:
4. **Interpretation of growth charts:**
  - a. Stunting: Length or height for age <5th percentile
  - b. Underweight:
    - (1) Children <3 years: weight for length <5th percentile
    - (2) Children  $\geq 2$  years: BMI for age <5th percentile
  - c. Healthy weight: BMI for age 5th percentile to <85th percentile
  - d. Overweight: Children >2 years: BMI for age 85th to <95th percentile
  - e. Obese:
    - (1) Children <3 years: Weight for length >95th percentile
    - (2) Children  $\geq 2$  years: BMI for age  $\geq 95$ th percentile
5. **Recommendations for management of overweight and obese children** (also see Figure EC 21-H on Expert Consult)<sup>3,4</sup>
  - a. Management is three-tiered focused on identification, assessment, and prevention:
    - (1) Identification: Calculate BMI at each well-child visit
    - (2) Assessment: Medical risk, behavior risk, and attitude
    - (3) Prevention: Targeted at behaviors and treatment interventions based on BMI stratification
  - b. Based on expert committee opinions, the Childhood Obesity Action Network has also developed an implementation guide for assessment and management of childhood obesity.<sup>5</sup>
6. **Growth charts:** For boys and girls, including weight, height, head circumference, BMI, and height velocity (see Figs. 21-1 to 21-9 and Figures EC 21-A to 21-G on Expert Consult). CDC recommends that clinicians in the United States use the 2006 WHO international growth charts rather than

**FIGURE EC 21-A**

Height velocity for girls ages 2–18 years. (Modified from Tanner JM, Davis PS. *Clinical longitudinal standards for height and height velocity in North American Children*. J Pediatr. 1985;107:317–329. Courtesy Castlemead Publications, 1985. Distributed by Serono Laboratories.)

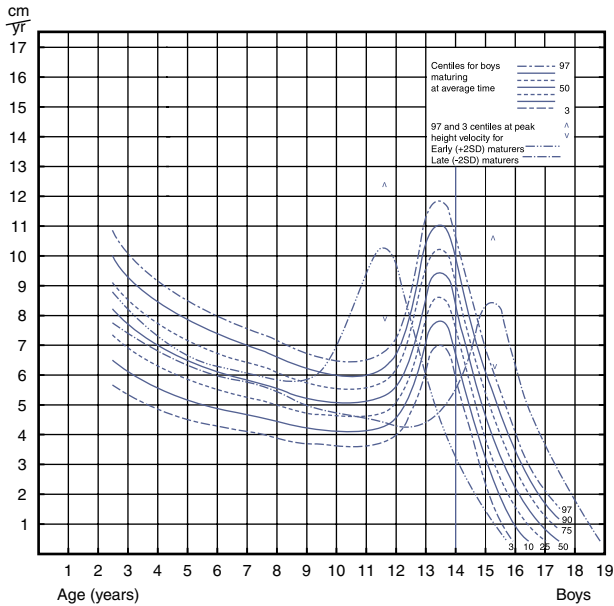
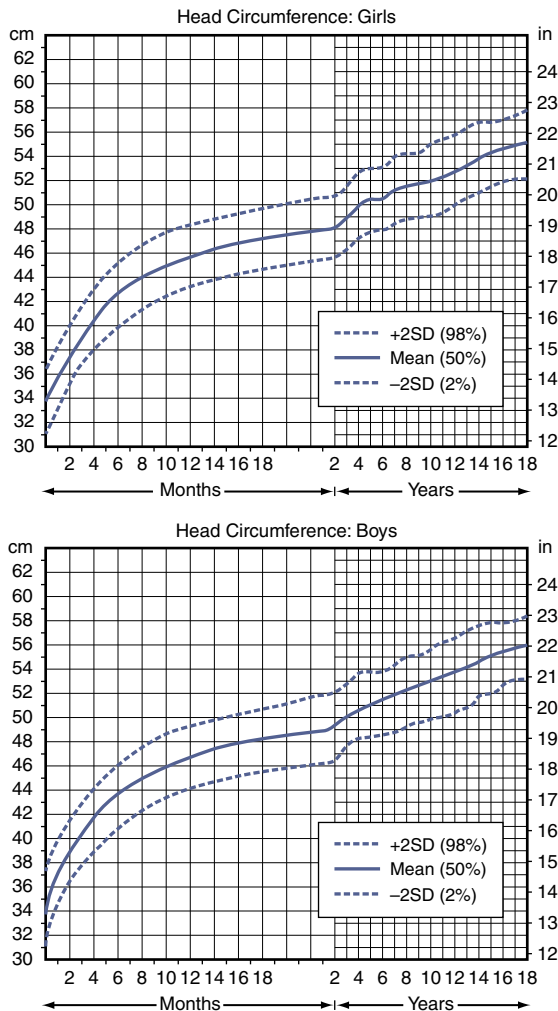


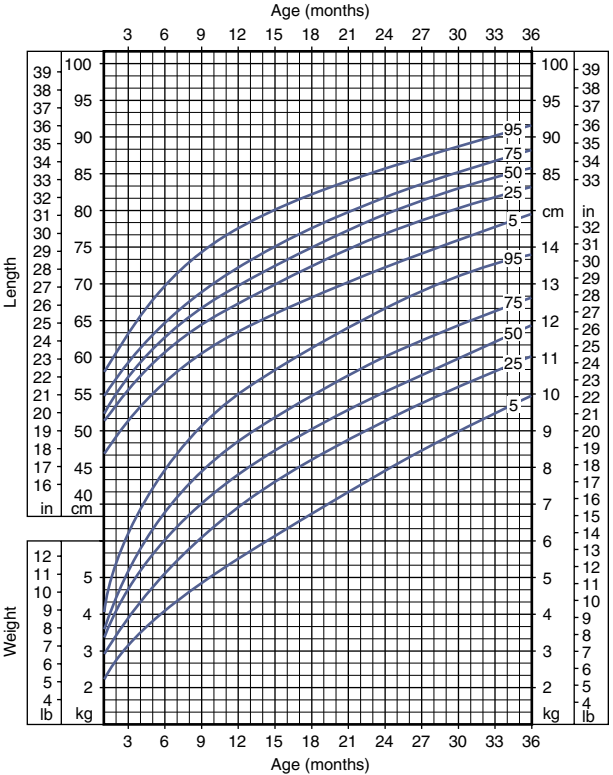
FIGURE EC 21-B

Height velocity for boys ages 2–18 years. (Modified from Tanner JM, Davis PS. *Clinical longitudinal standards for height and height velocity in North American Children*. [Data from Portland Health Institute, Inc., Portland, Oregon.] *J Pediatr*. 1985;107:317–329. Courtesy Castlemead Publications, 1985. Distributed by Serono Laboratories.)

**FIGURE EC 21-C**

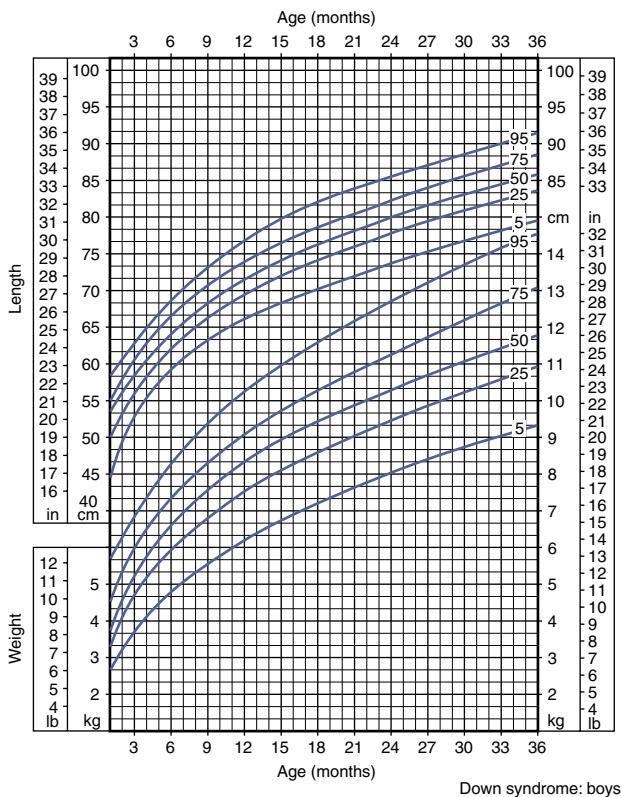
Head circumference for girls and boys ages 2–18 years. (Modified from Nelhaus G. *J Pediatr*. 1968;48:106.)



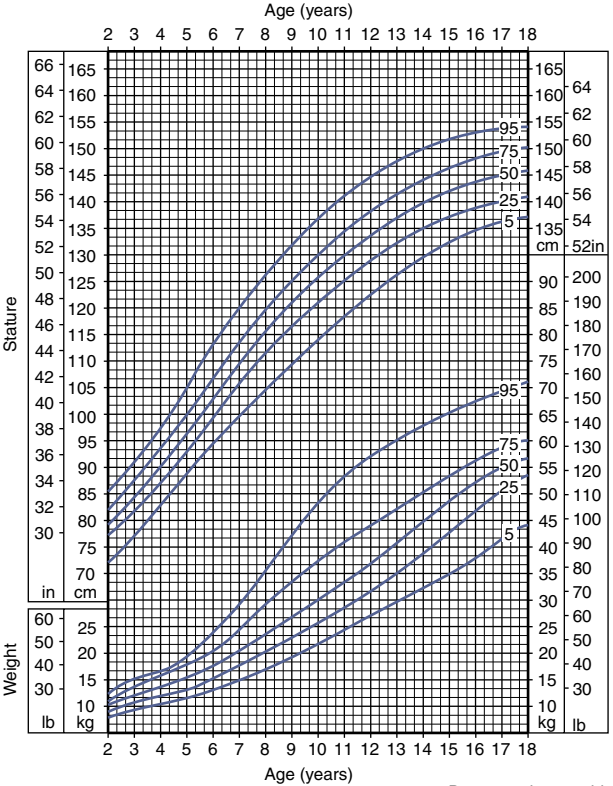


Down syndrome: girls

**FIGURE EC 21-D**  
Length and weight for girls with Down syndrome, birth to age 36 months. (Modified from Cronk C, Crocker AC, Pueschel SM, et al. Growth charts for children with Down syndrome: 1 month to 18 years of age. *Pediatrics*. 1988;81:102–110.)

**FIGURE EC 21-E**

Length and weight for boys with Down syndrome, birth to age 36 months. (Modified from Cronk C, Crocker AC, Pueschel SM, et al. Growth charts for children with Down syndrome: 1 month to 18 years of age. *Pediatrics*. 1988;81:102–110.)



Down syndrome: girls

FIGURE EC 21-F

Stature and weight for girls with Down syndrome, ages 2–18 years. (Modified from Cronk C, Crocker AC, Pueschel SM, et al. Growth charts for children with Down syndrome: 1 month to 18 years of age. *Pediatrics*. 1988;81:102–110.)

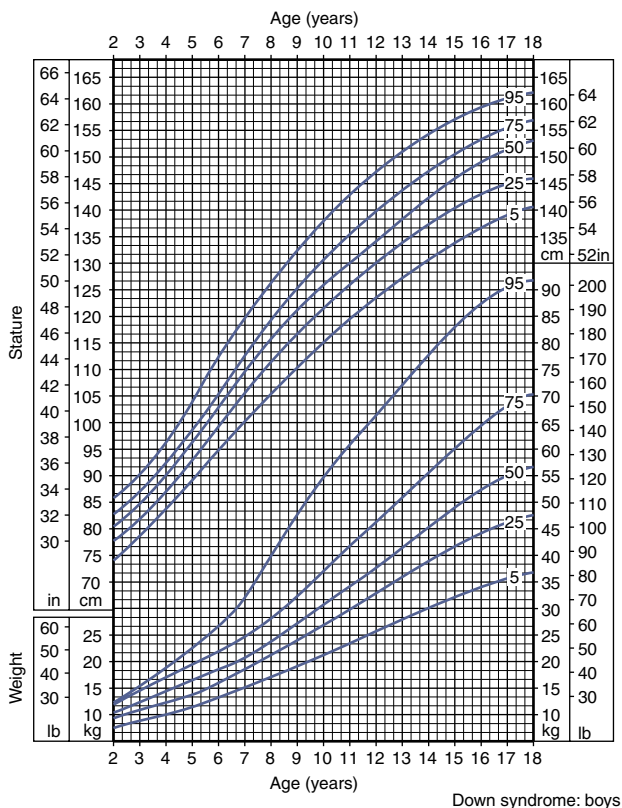
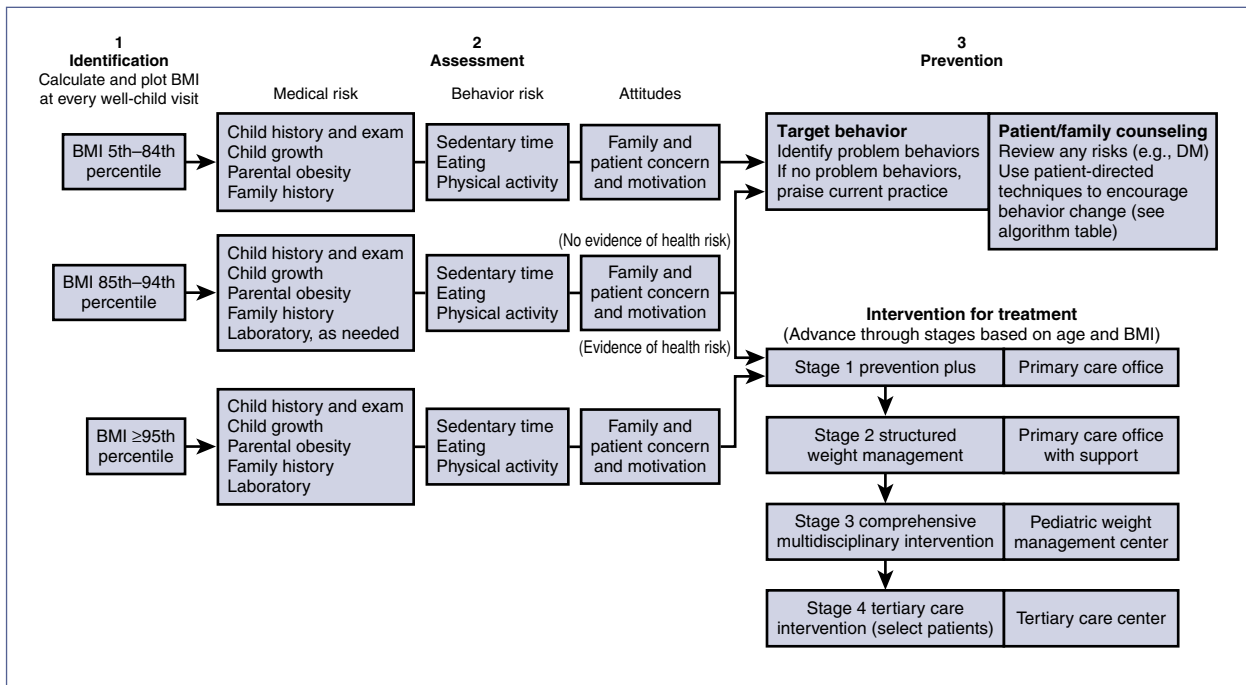


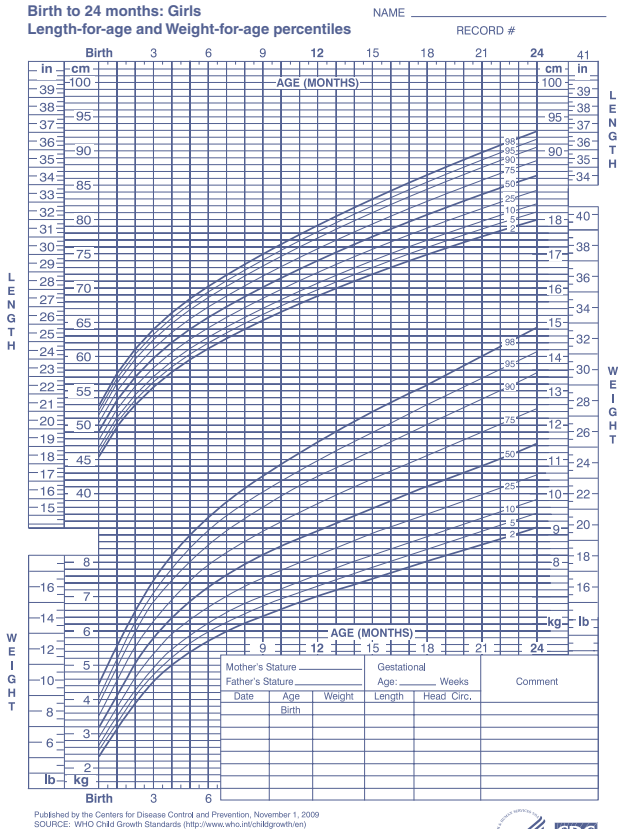
FIGURE EC 21-G

Stature and weight for boys with Down syndrome, ages 2–18 years. (Modified from Cronk C, Crocker AC, Pueschel SM, et al. Growth charts for children with Down syndrome: 1 month to 18 years of age. *Pediatrics*. 1988;81:102–110.)



**FIGURE EC 21-H**

Obesity decision tree. Recommendations for obesity management. BMI, Body mass index; DM, diabetes mellitus. (Redrawn from Barlow SE; Expert Committee. Expert Committee recommendations regarding the prevention, assessment, and treatment of child and adolescent overweight and obesity: summary report. Pediatrics. 2007;120:S164–S192.)

**FIGURE 21-1**

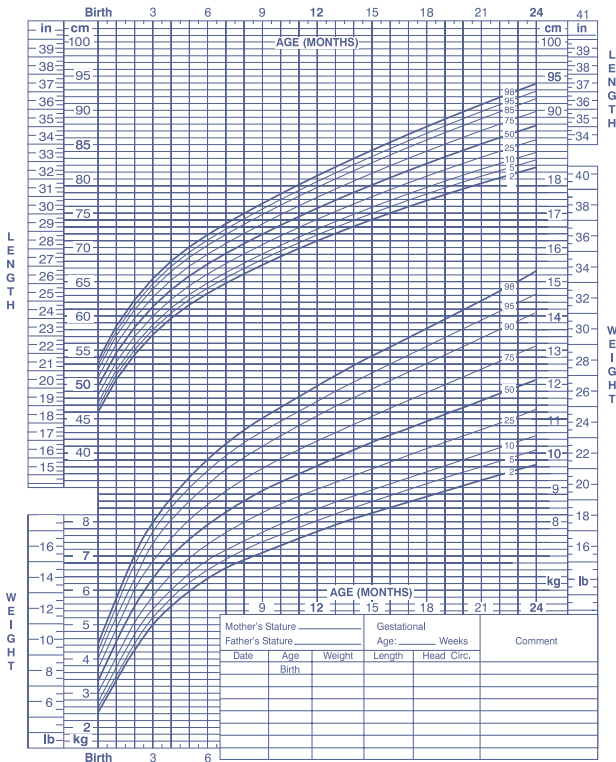
Length and weight for girls, birth to age 24 months. (Published by the Centers for Disease Control and Prevention, November 1, 2009. SOURCE: WHO Child Growth Standards [<http://www.who.int/childgrowth/en>].)



**Birth to 24 months: Boys**  
**Length-for-age and Weight-for-age percentiles**

NAME \_\_\_\_\_

RECORD # \_\_\_\_\_



Published by the Centers for Disease Control and Prevention, November 1, 2009  
 SOURCE: WHO Child Growth Standards (<http://www.who.int/childgrowth/en>)


**FIGURE 21-3**

Length and weight for boys, birth to age 24 months. (Published by the Centers for Disease Control and Prevention, November 1, 2009. SOURCE: WHO Child Growth Standards [<http://www.who.int/childgrowth/en>].)





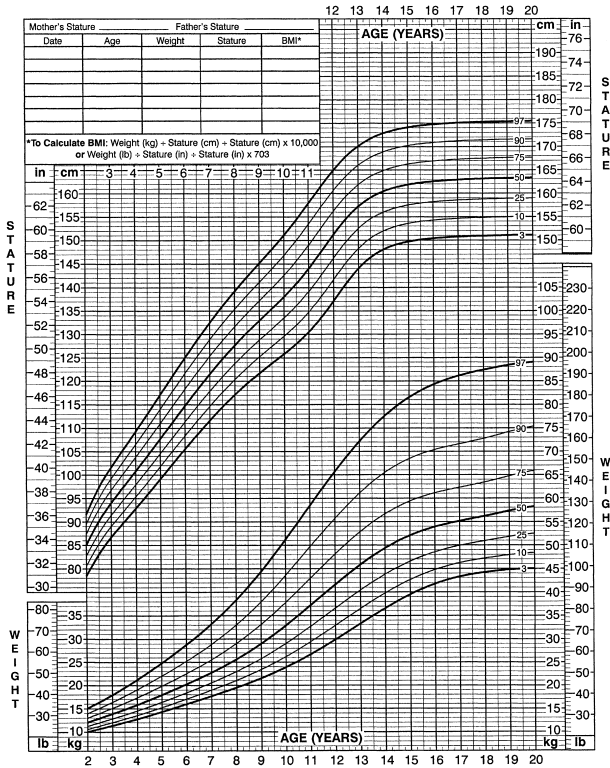
Head circumference and length-to-weight ratio for boys, birth to age 24 months. (Published by the Centers for Disease Control and Prevention, November 1, 2009. SOURCE: WHO Child Growth Standards [<http://www.who.int/childgrowth/en>].)

### 2 to 20 years: Girls

NAME \_\_\_\_\_

### Stature-for-age and Weight-for-age percentiles

RECORD # \_\_\_\_\_

**FIGURE 21-5**

Stature and weight for girls ages 2–20 years. (Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion, 2000.)



### 2 to 20 years: Boys

NAME \_\_\_\_\_

### Stature-for-age and Weight-for-age percentiles

RECORD # \_\_\_\_\_

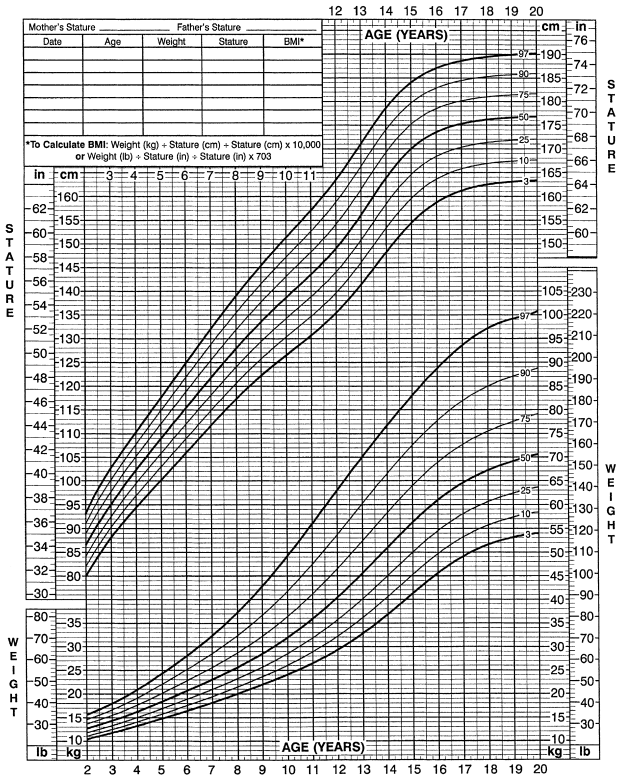
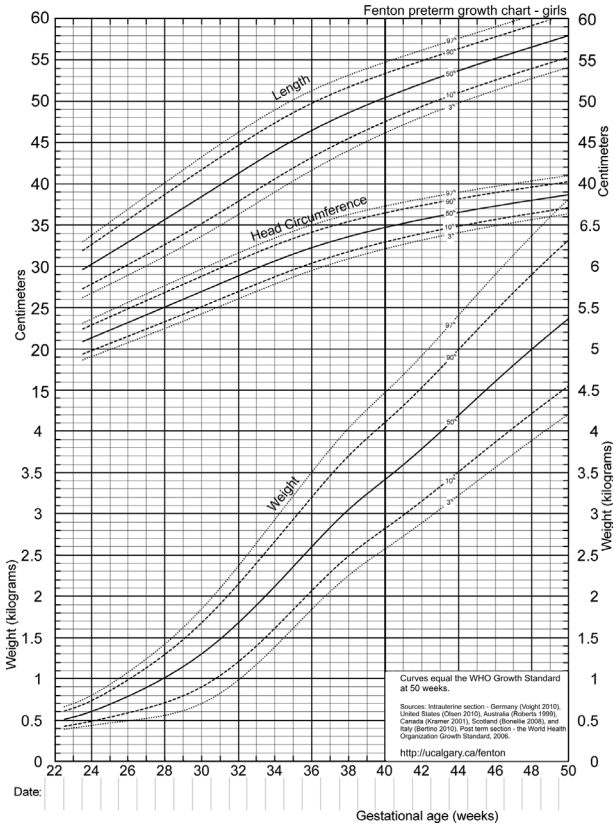


FIGURE 21-7

Stature and weight for boys ages 2–20 years. (Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion, 2000.)



**FIGURE 21-9**

Length, weight, and head circumference for preterm infants. (From Fenton RT, Kim HJ. A systematic review and meta-analysis to revise the Fenton growth chart for preterm infants. BMC Pediatrics. 2013, 13:59.)

Continued

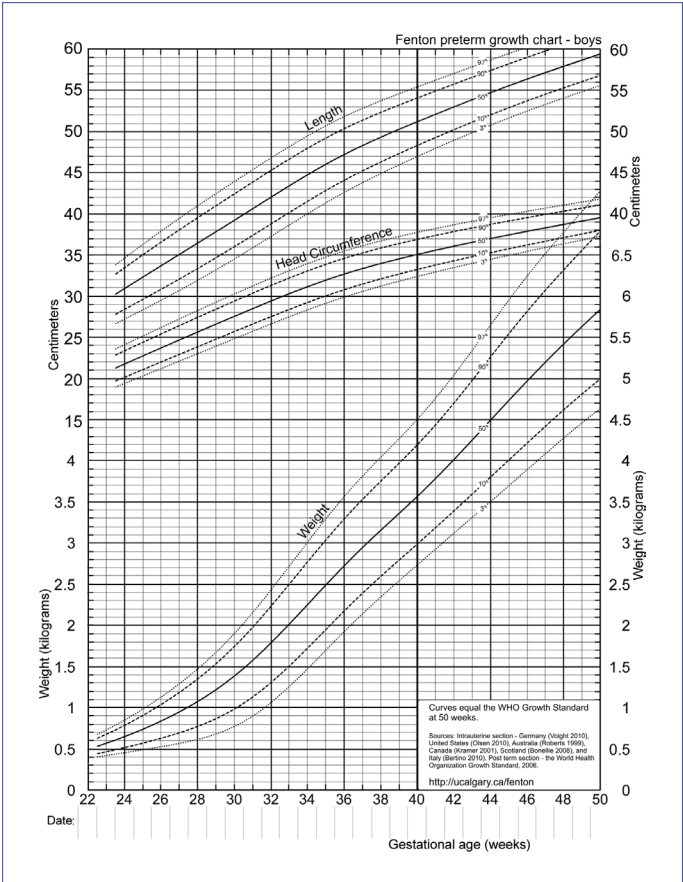


FIGURE 21-9, cont'd

the CDC growth charts for children aged <24 months. Growth charts for children ages 0–20 years, including 2000 CDC growth charts for ages 0–36 months and 2006 WHO growth charts for ages 0–24 months, can be downloaded from <http://www.cdc.gov/growthcharts/>

#### 7. **Growth charts for special populations:**

- a. Down syndrome: <http://www.ndss.org>; follow links to health care and growth charts (also see [Figures EC 21-D to 21-G](#) on Expert Consult)
- b. Turner syndrome: <http://aappolicy.aappublications.org/cgi/content/full/pediatrics;111/3/692/F1>
- c. Achondroplasia: <http://aappolicy.aappublications.org/cgi/content/full/pediatrics;116/3/771>
8. **Waist circumference and waist/height ratio:** Both waist circumference (WC) and waist/height ratio are indicators of visceral fat or abdominal obesity in children and adolescents aged 2–19 years. Increased visceral adiposity measured by WC increases the risk of obesity-related morbidity and mortality. WC should be measured at the high point of the iliac crest when the individual is standing and at minimal respiration. Waist/height ratio is calculated as a ratio of waist circumference (cm) and height (cm).<sup>6</sup> See CDC waist circumference tables for individuals ages 2–19 years: <http://www.cdc.gov/nchs/data/nhsr/nhsr010.pdf>, Table 18

### III. ESTIMATING ENERGY NEEDS

#### A. Definitions of Energy Needs<sup>2</sup>

1. **Basal metabolic rate (BMR):** Rate of energy expenditure after an overnight fast, resting comfortably, supine, awake, and motionless in a thermoneutral environment.
2. **Basal energy expenditure (BEE):** BMR over 24 hours.
3. **Thermic effect of food (TEF):** Increase in energy expenditure elicited by food consumption.
4. **Energy deposition:** Energy requirement for growth.
5. **Total energy expenditure (TEE):** Sum of BEE, TEF, physical activity, thermoregulation, and energy expended in depositing new tissues and/or producing milk.
6. **Physical activity level (PAL):** Ratio of total to basal daily energy expenditure (TEE/BEE). Describes and accounts for physical activity habits.
7. **Physical activity coefficient (PA):** The physical activity coefficient that correlates with PAL ([Table 21-1](#)) can be used to calculate estimated energy requirements (EER [see [Section III.B](#)]).

#### B. Estimated Energy Requirements<sup>2</sup>

1. **EER:** Dietary energy intake predicted to maintain energy balance in a healthy individual. In children, EER includes the needs associated with growth. For most healthy infants and children, the equations here can be used to determine energy needs.
- a. For infants, children, and adolescents,  $EER \text{ (kcal/day)} = TEE + \text{energy deposition}$



TABLE 21-1

## PHYSICAL ACTIVITY COEFFICIENTS

	Sedentary Activity (Physical Activity Levels Required for Independent Living)	Low Active (30–45 min Sustained Daily Activity)	Active (60 min Sustained Daily Activity)	Very Active ( $\geq 90$ min Sustained Daily Activity)
PAL	$\geq 1.0$ but $< 1.4$	$\geq 1.4$ but $< 1.6$	$\geq 1.6$ but $< 1.9$	$\geq 1.9$ but $< 2.5$
PA (boys ages 3–18)	1.00	1.13	1.26	1.42
PA (girls ages 3–18)	1.00	1.16	1.31	1.56

PA, Physical activity coefficient; PAL, physical activity level.

- b. For most hospitalized patients, it can be assumed PAL = sedentary,  
PA = 1

2. **EER equations (calculate calories/day):**

a. **Infants and young children:**

- (1) 0–3 months:  $EER = (89 \times \text{weight [kg]} - 100) + 175$
- (2) 4–6 months:  $EER = (89 \times \text{weight [kg]} - 100) + 56$
- (3) 7–12 months:  $EER = (89 \times \text{weight [kg]} - 100) + 22$
- (4) 13–35 months:  $EER = (89 \times \text{weight [kg]} - 100) + 20$

b. **Boys ages 3–18:**

- (1) 3–8 years:  $EER = 88.5 - (61.9 \times \text{age [yr]}) + (PA \times 26.7 \times \text{weight [kg]}) + (903 \times \text{height [m]}) + 20$
- (2) 9–18 years:  $EER = 88.5 - (61.9 \times \text{age [yr]}) + (PA \times 26.7 \times \text{weight [kg]}) + (903 \times \text{height [m]}) + 25$

c. **Girls ages 3–18:**

- (1) 3–8 years:  $EER = 135.3 - (30.8 \times \text{age [yr]}) + (PA \times 10 \times \text{weight [kg]}) + (934 \times \text{height [m]}) + 20$
- (2) 9–18 years:  $EER = 135.3 - (30.8 \times \text{age [yr]}) + (PA \times 10 \times \text{weight [kg]}) + (934 \times \text{height [m]}) + 25$

d. **Pregnancy (14–18 years):**  $EER = \text{adolescent EER} + \text{pregnancy energy deposition}$ :

- (1) First trimester = adolescent EER + 0 kcal
- (2) Second trimester = adolescent EER + 340 kcal
- (3) Third trimester = adolescent EER + 452 kcal

e. **Lactation (14–18 years):**  $EER = \text{adolescent EER} + \text{milk energy output} - \text{weight loss}$ :

- (1) First 6 months = adolescent EER + 500 – 170
- (2) Second 6 months = adolescent EER + 400 – 0

3. [Table 21-22](#) contains the estimated EER for healthy boys and girls of median weight (weight for age at 50th percentile) at both sedentary and active PAL levels.

**C. EER Under Stressed Conditions<sup>7</sup>**

**Calculation of BEE:** In many cases, there is little need to provide critically ill patients with more than their BEE. Ideally, energy expenditure should

TABLE 21-2

## SAMPLE ESTIMATED ENERGY REQUIREMENTS FOR HEALTHY BOYS AND GIRLS OF MEDIAN WEIGHT AND HEIGHT\*

Age	Boys EER (kcal/kg/day)			Girls EER (kcal/kg/day)		
0–2 mo	107			104		
3 mo	95			95		
4–35 mo	82			82		
	Boys			Girls		
	Median Weight, Boys (kg)	Sedentary† (kcal/kg/d)	Active† (kcal/kg/d)	Median Weight, Girls (kg)	Sedentary† (kcal/kg/d)	Active† (kcal/kg/d)
3 yr	14.3	80	104	13.9	76	100
4 yr	16.2	74	97	15.8	70	93
5 yr	18.4	68	90	17.9	65	87
6 yr	20.7	63	84	20.2	61	81
7 yr	23.1	59	80	22.8	56	75
8 yr	25.6	56	75	25.6	52	71
9 yr	28.6	53	71	29.0	48	65
10 yr	31.9	49	67	32.9	44	60
11 yr	35.9	46	63	37.2	41	56
12 yr	40.5	44	60	41.6	38	52
13 yr	45.6	42	57	45.8	36	50
14 yr	51.0	40	55	49.4	34	47
15 yr	56.3	39	54	52.0	33	45
16 yr	60.9	38	52	53.9	32	44
17 yr	64.6	36	50	55.1	31	43
18 yr	67.2	35	49	56.2	30	42

\*Weight and height for age at 50th percentile.

†See definition of sedentary and active PAL for further information.

EER, Estimated energy requirements.

From Otten JJ, Hellwig JP, Meyers LD, eds. *Dietary Reference Intakes: The Essential Guide to Nutrient Requirements*.

Washington, DC: National Academies Press, 2006.

be measured in critically ill patients, but this requires expensive equipment and may not always be practical. Numerous prediction equations are available, and the following is from the *Dietary Reference Intakes*<sup>7</sup>:

For boys:  $BEE \text{ (kcal/d)} = 68 - (43.3 \times \text{age [yr]}) + (712 \times \text{height [m]}) + (19.2 \times \text{weight [kg]})$

For girls:  $BEE \text{ (kcal/d)} = 189 - (17.6 \times \text{age [yr]}) + (625 \times \text{height [m]}) + (7.9 \times \text{weight [kg]})$

Appropriate changes should be made as indicated by real (not fluid) weight gain and signs and symptoms of overfeeding.

#### D. Catch-up Growth Requirement for Malnourished Infants and Children (<3 years)<sup>8,9</sup>

1. **Growth failure** (also known as *failure to thrive*): Condition of undernutrition generally identified in the first 3 years of life. Can be described by

## BOX 21-1

**DETERMINING CATCH-UP GROWTH REQUIREMENTS**

1. Plot the child's height and weight on CDC growth charts.
2. Determine recommended calories needed for age (recommended dietary allowances [RDA]).
3. Determine the ideal weight (50th percentile) for child's height.\*
4. Multiply the RDA calories by ideal body weight for height (kg).
5. Divide this value by the child's actual weight (kg).

For example, for a 12-month-old boy whose weight is 7 kg and length is 72 cm, RDA for age would be 98 kcal/kg/day, and ideal body weight for height is 9 kg (50th percentile weight for height). Thus his catch-up growth requirement would be as follows:

$$98 \text{ kcal/kg/day} \times (9 \text{ kg}/7 \text{ kg}) = 126 \text{ kcal/kg/day.}$$

\*Ideal weight can be 10th–85th percentile weight for height, depending on past growth trends; clinical judgment should be used.

the following growth scenarios: Weight for age <5th percentile on the CDC growth charts, weight for length (or height) <5th percentile, or decreased growth velocity resulting in weight falling >2 major percentiles over 3–6 months (**NOTE:** WHO growth charts have been recently recommended by the CDC for children <24 months, and one may consider using these charts to define growth failure.)

2. **Catch-up growth:** Time period of accelerated growth as a result of caloric provision in excess of the recommended dietary allowances (RDAs). Approximately 20%–30% more energy may be required to achieve catch-up growth in children. Protein needs also increase. This should continue until the previous growth percentiles are regained. Catch-up in linear growth may lag several months behind that in weight. [Box 21-1](#) lists the steps for determining catch-up growth requirements

**NOTE:** Aggressive refeeding in the severely malnourished child can result in metabolic alterations, vomiting, diarrhea, and circulatory decompensation known as *refeeding syndrome* (hypophosphatemia, hypokalemia, hypomagnesemia, and glucose and/or fluid intolerance).<sup>10</sup>

## IV. DIETARY REFERENCE INTAKES FOR INDIVIDUALS

### A. Dietary Reference Intakes

Dietary reference intakes (DRIs) are reference values based on quantitative estimates of nutrient intakes and measured in several ways:

1. **Estimated average requirement (EAR):** Daily nutrient intake level estimated to meet the requirement of half the healthy individuals in a particular life stage and gender group.
2. **Recommended dietary allowance (RDA):**  $\text{EAR} \pm 2$  standard deviations. The daily nutrient intake level estimated to meet the requirement of 97%–98% of healthy individuals in a particular life stage and gender group.
3. **Adequate intake (AI):** Observed range of intakes in a healthy population; used when data are insufficient to calculate EAR and RDA.

4. **Tolerable upper intake level (UL):** Highest daily nutrient intake level likely to pose no risk for adverse health effects to almost all individuals in the general population.

### B. Protein Requirements (Table 21-3)<sup>7</sup>

### C. Fat Requirements (Table 21-4)<sup>7</sup>

### D. Vitamin Requirements (Table 21-5)<sup>7</sup>

#### 1. Vitamin D supplementation

- a. Breast-fed and partially breast-fed infants: Should be supplemented with 400 IU/day of vitamin D beginning in the first few days of life.

TABLE 21-3

#### PROTEIN REQUIREMENTS

Age	RDA (g/kg/day)
0–6 mo	1.52 (AI)*
7–12 mo	1.2
1–3 yr	1.05
4–8 yr	0.95
9–13 yr	0.95
14–18 yr	0.85
Pregnancy (first half)	Unchanged
Pregnancy (second half)	1.1
Lactation	1.3

\*If sufficient scientific evidence is not available to establish RDA (recommended dietary allowance), an AI (adequate intake) is usually developed. For healthy breast-fed infants, the AI is the mean intake.

From Otten JJ, Hellwig JP, Meyers LD, eds. *Dietary Reference Intakes: The Essential Guide to Nutrient Requirements*. Washington, DC: National Academies Press, 2006.

TABLE 21-4

#### FAT REQUIREMENTS: ADEQUATE INTAKE (AI)\*

Age	Total Fat (g/day)	Linoleic Acid (g/day)	$\alpha$ -Linolenic Acid (g/day)
0–6 mo	31	4.4 (n-6 PUFA)	0.5 (n-3 PUFA)
7–12 mo	30	4.6 (n-6 PUFA)	0.5 (n-3 PUFA)
1–3 yr	†	7	0.7
4–8 yr	†	10	0.9
9–13 yr, boys	†	12	1.2
9–13 yr, girls	†	10	1.0
14–18 yr, boys	†	16	1.6
14–18 yr, girls	†	11	1.1
Pregnancy	†	13	1.4
Lactation	†	13	1.3

\*If sufficient scientific evidence is not available to establish RDA (recommended dietary allowance), an AI (adequate intake) is usually developed. For healthy breast-fed infants, the AI is the mean intake. The AI for other life stage and gender groups is believed to cover the needs of all healthy individuals in the group, but a lack of data or uncertainty in the data prevents being able to specify with confidence the percentage of individuals covered by this intake.

†No AI, estimated average requirement (EAR), or RDA established.

PUFA, Polyunsaturated fatty acid.

From Otten JJ, Hellwig JP, Meyers LD, eds. *Dietary Reference Intakes: The Essential Guide to Nutrient Requirements*. Washington, DC: National Academies Press, 2006.

TABLE 21-5

## DIETARY REFERENCE INTAKES: RECOMMENDED INTAKES FOR INDIVIDUALS—VITAMINS

Life Stage	Vit. A <sup>a</sup> (IU)	Vit. C (mg/day)	Vit. D <sup>b,c</sup> (IU)	Vit. E <sup>d</sup> (IU)	Vit. K (mcg/day)	Thiamin (mg/day)	Riboflavin (mg/day)	Niacin <sup>e</sup> (mg/day)	Vit. B <sub>6</sub> (mg/day)	Folate <sup>f</sup> (mcg/day)	Vit. B <sub>12</sub> (mcg/day)	Pantothenic Acid (mg/day)	Biotin (mcg/day)	Choline <sup>g</sup> (mg/day)
<b>INFANTS</b>														
0–6 mo	1333	40*	400	4*	2.0*	0.2*	0.3*	2*	0.1*	65*	0.4*	1.7*	5*	125*
7–12 mo	1666	50*	400	5*	2.5*	0.3*	0.4*	4*	0.3*	80*	0.5*	1.8*	6*	150*
<b>CHILDREN</b>														
1–3 yr	1000	15	600	6	30*	0.5	0.5	6	0.5	150	0.9	2*	8*	200*
4–8 yr	1333	25	600	7	55*	0.6	0.6	8	0.6	200	1.2	3*	12*	25*
<b>MALES</b>														
9–13 yr	2000	45	600	11	60*	0.9	0.9	12	1.0	300	1.8	4*	20*	375*
14–18 yr	3000	75	600	15	75*	1.2	1.3	16	1.3	400	2.4	5*	25*	550*
19–30 yr	3000	90	600	15	120*	1.2	1.3	16	1.3	400	2.4	5*	30*	550*
<b>FEMALES</b>														
9–13 yr	2000	45	600	11	60*	0.9	0.9	12	1.0	300	1.8	4*	20*	375*
14–18 yr	2333	65	600	15	75*	1.0	1.0	14	1.2	400	2.4	5*	25*	400*
19–30 yr	2333	75	600	15	90*	1.1	1.1	14	1.3	400	2.4	5*	30*	425*

**PREGNANCY**

<18 yr	<b>2500</b>	<b>80</b>	600	<b>15</b>	75*	<b>1.4</b>	<b>1.4</b>	<b>18</b>	<b>1.9</b>	<b>600</b>	2.6	6*	30*	450*
19–30 yr	<b>2567</b>	<b>85</b>	600	<b>15</b>	90*	<b>1.4</b>	<b>1.4</b>	<b>18</b>	<b>1.9</b>	<b>600</b>	2.6	6*	30*	450*

**LACTATION**

<18 yr	<b>4000</b>	<b>115</b>	600	<b>19</b>	75*	<b>1.4</b>	<b>1.6</b>	<b>17</b>	<b>2.0</b>	<b>500</b>	2.8	7*	35*	550*
19–30 yr	<b>4333</b>	<b>120</b>	600	<b>19</b>	90*	<b>1.4</b>	<b>1.6</b>	<b>17</b>	<b>2.0</b>	<b>500</b>	2.8	7*	35*	550*

\*One International Unit (IU) = 0.3 mcg retinol equivalent.

<sup>b</sup>One mcg cholecalciferol = 40 IU vitamin D.

<sup>c</sup>In the absence of adequate exposure to sunlight.

<sup>d</sup>One IU = 1 mg vitamin E.

<sup>e</sup>As niacin equivalents (NE). 1 mg of niacin = 60 mg of tryptophan; 0–6 months = preformed niacin (not NE).

<sup>f</sup>As dietary folate equivalents (DFE). 1 DFE = 1 mcg food folate = 0.6 mcg of folic acid from fortified food or as a supplement consumed with food = 0.5 mcg of a supplement taken on an empty stomach. In view of evidence linking folate intake with neural tube defects in the fetus, it is recommended that all women capable of becoming pregnant consume 400 mcg from supplements or fortified foods in addition to intake of food folate from a varied diet. It is assumed that women will continue consuming 400 mcg from supplements or fortified food until their pregnancy is confirmed and they enter prenatal care, which ordinarily occurs after the end of the periconceptual period—the critical time for formation of the neural tube.

<sup>g</sup>Although AIs have been set for choline, there are few data to assess whether a dietary supply of choline is needed at all life stages, and it may be that the choline requirement can be met by endogenous synthesis at some of these stages.

**NOTE:** This table (taken from the DRI reports; see [www.nap.edu](http://www.nap.edu)) presents recommended dietary allowances (RDAs) in **bold type** and adequate intakes (AIs) in regular type followed by an asterisk (\*). RDAs and AIs may both be used as goals for individual intake. RDAs are set to meet the needs of almost all (97%–98%) individuals in a group. For healthy breast-fed infants, the AI is the mean intake. The AI for other life stage and gender groups is believed to cover needs of all individuals in the group, but lack of data or uncertainty in the data prevent being able to specify with confidence the percentage of individuals covered by this intake.

Modified from Otten JJ, Hellwig JP, Meyers LD, eds. *Dietary Reference Intakes: The Essential Guide to Nutrient Requirements*. Washington, DC: National Academies Press, 2006.

Supplementation should be continued unless the infant is taking 1000 mL/day of vitamin D–fortified formula.

- b. Infants not breast-fed and older children: If ingesting <1000 mL/day of vitamin D–fortified formula, fortified foods, or milk, should receive supplementation of 400 IU/day
- c. Adolescents: If not obtaining 600 IU of vitamin D through fortified milk (100 IU per 8-oz serving) and fortified food (fortified cereals, egg yolks), should be supplemented with 600 IU/day

**2. Examples of multivitamins for infants and children (Tables 21-6 and 21-7)**

**E. Mineral Requirements (Table 21-8)<sup>7</sup>**

**1. Iron supplementation**

- a. Breast-fed term infants: Should receive 1 mg/kg of an oral iron supplement beginning at 4 months of age, preferably from iron-fortified cereal or, alternatively, elemental iron
- b. Breast-fed preterm infants: Should receive 2 mg/kg/day by 1 month of age, which should be continued until the infant is weaned to iron-fortified formula or begins eating complementary foods
- c. Formula-fed term infants: Receive adequate iron from fortified formula (4–12 mg/L) from birth to age 12 months
- d. Formula-fed preterm infants: Need an additional supplementation of 1 mg/kg/day to get total daily dose of 2 mg/kg/day

**2. Fluoride supplementation**

- a. Supplementation not needed during the first 6 months of life. Thereafter, 0.5 mg/day is recommended for exclusively breast-fed infants.

**TABLE 21-6**

**INFANT MULTIVITAMIN DROPS ANALYSIS (PER ML)\***

Nutrient	Poly-Vi-Sol [w/iron], Multivitamin [with iron]	Tri-Vi-Sol [w/iron]	AquaDEKs†‡	D Vi-Sol	Fer-In-Sol
Vitamin A (IU)	1500	1500	5751	—	—
Vitamin D (IU)	400	400	400	400	—
Vitamin E (IU)	5	—	50	—	—
Vitamin C (mg)	35	35	45	—	—
Thiamin (mg)	0.5	—	0.6	—	—
Riboflavin (mg)	0.6	—	0.6	—	—
Niacin (mg)	8	—	6	—	—
Vitamin B <sub>6</sub> (mg)	0.4	—	0.6	—	—
Vitamin B <sub>12</sub> (mcg)	2	—	—	—	—
Vitamin K (mcg)	—	—	400	—	—
Iron (mg)	[10]	[10]	—	—	15
Fluoride (mg)	—	—	—	—	—
Zinc (mg)	—	—	5	—	—

\*Standard dose = 1 mL.

†Also contains biotin 15 mcg; pantothenic acid 3 mg; 87% vitamin A as  $\beta$ -carotene; coenzyme Q<sub>10</sub> 2 mg; selenium 10 mcg.

‡Recommended for use in infants with fat malabsorption, such as cystic fibrosis, liver disease.

TABLE 21-7

## MULTIVITAMIN TABLETS (ANALYSIS/TABLET)

	Flintstones Sour Gummies	Centrum Kids Complete	Flintstones Complete	Centrum Tablet*	AquADEKs (Softgel)	Source CF (Chewable)	Vitamax (Chewable)	Phlexy-Vits (7-g Packet)	Nano-VM 1–3 yrs. (2 Scoops)	Nano-VM 4–8 yrs. (2 Scoops)
Vitamin A (IU)	1000	3500	3000	3500	18,167	16,000 <sup>a</sup>	5000 <sup>b</sup>	2664	1000	1332
Vitamin D (IU)	100	400	400	400	800	1,000	400	400	400	400
Vitamin E (IU)	10	30	30	30	150	200	200	13.5	9	10
Vitamin K (mcg)	—	10	—	25	700	800	200	70	30	55
Vitamin C (mg)	15	60	60	60	75	100	60	50	15	25
Thiamin (mg)	—	1.5	1.5	1.5	1.5	1.5	1.5	1.2	0.5	0.6
Riboflavin (mg)	—	1.7	1.7	1.7	1.7	1.7	1.7	1.4	0.5	0.6
Niacin (mg)	—	20	15	20	20	10	20	20	6	8
Vitamin B <sub>6</sub> (mg)	0.5	2	2	2	1.9	1.9	2	1.6	0.5	0.6
Folate (mcg)	100	400	400	400	200	200	200	700	150	200
Vitamin B <sub>12</sub> (mcg)	2.5	6	6	6	12	6	6	5	0.9	1.2
Biotin (mcg)	38	45	40	30	100	100	300	150	8	12
Pantothenic acid (mg)	2.5	10	10	10	12	12	10	5	2	3
Calcium (mg)	—	108	100	200	—	—	—	1,000	500	800
Phosphorus (mg)	—	50	100	20	—	—	—	775	460	500
Iron (mg)	—	18	18	18	—	—	—	15.1	7	10

Continued



TABLE 21-7

## MULTIVITAMIN TABLETS (ANALYSIS/TABLET) (Continued)

	Flintstones Sour Gummies	Centrum Kids Complete	Flintstones Complete	Centrum Tablet <sup>a</sup>	AquaDEKs (Softgel)	Source CF (Chewable)	Vitamax (Chewable)	Phlexy-Vits (7-g Packet)	Nano-VM 1–3 yrs. (2 Scoops)	Nano-VM 4–8 yrs. (2 Scoops)
Iodine (mcg)	20	150	150	150	—	—	—	150	90	90
Magnesium (mg)	—	40	20	50	—	—	—	300	65	110
Zinc (mg)	1.2	15	12	11	10	15	7.5	11.1	3	5
Copper (mg)	—	2	2	0.5	—	—	—	1.5	0.34	0.44
Manganese (mg)	—	1	—	2.3	—	—	—	1.5	1.2	1.5
Chromium (mcg)	—	20	—	35	—	—	—	30	11	15
Molybdenum (mcg)	—	20	—	45	—	—	—	70	17	22
Selenium (mcg)	—	—	—	55	75	—	—	75	20	30
Fluoride (mg)	—	—	—	—	—	—	—	—	—	—
Choline (mg)	38	—	38	—	—	—	—	—	—	—
Sodium (mg)	—	—	10	—	—	—	—	8.8	0	0
Potassium (mg)	—	—	—	80	—	—	—	<1.4	575	775
Chloride	—	—	—	72	—	—	—	<0.35	0	0

<sup>a</sup>Contains boron, nickel, silicon, tin.

<sup>a</sup> Vitamin A: 88% β-carotene, 12% palmitate.

<sup>b</sup> Vitamin A as acetate and 50% β-carotene.

TABLE 21-8

## DIETARY REFERENCE INTAKES: RECOMMENDED INTAKES—ELEMENTS

Life Stage	Calcium (mg/day)	Chromium (mcg/day)	Copper (mcg/day)	Fluoride (mg/day)	Iodine (mcg/day)	Iron (mg/day)	Magnesium (mg/day)	Manganese (mg/day)	Molybdenum (mcg/day)	Phosphorus (mg/day)	Selenium (mcg/day)	Zinc (mg/day)
<b>INFANTS</b>												
0–6 mo	200*	0.2*	200*	0.01*	110*	0.27*	30*	0.003*	2*	100*	15*	2*
7–12 mo	260*	5.5*	220*	0.5*	130*	11	75*	0.6*	3*	275*	20*	3
<b>CHILDREN</b>												
1–3 yr	700	11*	340	0.7*	90	7	80	1.2*	17	460	20	3
4–8 yr	1000	15*	440	1.0*	90	10	130	1.5*	22	500	30	5
<b>MALES</b>												
9–13 yr	1300	25*	700	2*	120	8	240	1.9*	34	1250	40	8
14–18 yr	1300	35*	890	3*	150	11	410	2.2*	43	1250	55	11
19–30 yr	1000	35*	900	4*	150	8	400	2.3*	45	700	55	11

*Continued*

TABLE 21-8

## DIETARY REFERENCE INTAKES: RECOMMENDED INTAKES—ELEMENTS (Continued)

Life Stage	Calcium (mg/day)	Chromium (mcg/day)	Copper (mcg/day)	Fluoride (mg/day)	Iodine (mcg/day)	Iron (mg/day)	Magnesium (mg/day)	Manganese (mg/day)	Molybdenum (mcg/day)	Phosphorus (mg/day)	Selenium (mcg/day)	Zinc (mg/day)
<b>FEMALES</b>												
9–13 yr	1300	21*	700	2*	120	8	240	1.6*	34	1250	40	8
14–18 yr	1300	24*	890	3*	150	15	360	1.6*	43	1250	55	9
19–30 yr	1000	25*	900	3*	150	18	310	1.8*	45	700	55	8
<b>PREGNANCY</b>												
<18 yr	1300	29*	1000	3*	220	27	400	2.0*	50	1250	60	13
19–30 yr	1000	30*	1000	3*	220	27	350	2.0*	50	700	60	11
<b>LACTATION</b>												
<18 yr	1300	44*	1300	3*	290	10	360	2.6*	50	1250	70	14
19–30 yr	1000	45*	1300	3*	290	9	310	2.6*	50	700	70	12

**NOTE:** This table presents recommended dietary allowances (RDAs) in **bold type** and adequate intakes (AIs) in ordinary type followed by an asterisk (\*). RDAs and AIs may both be used as goals for individual intake.

RDAs are set to meet the needs of almost all (97%–98%) individuals in a group. For healthy breast-fed infants, the AI is the mean intake. The AI for other life stage and gender groups is believed to cover needs of all individuals in the group, but lack of data or uncertainty in the data prevent being able to specify with confidence the percentage of individuals covered by this intake.

Modified from Otten JJ, Hellwig JP, Meyers LD, eds. *Dietary Reference Intakes: The Essential Guide to Nutrient Requirements*. Washington, DC: National Academies Press; 2006. Includes updates from. Ross AC, Taylor CL, Yaktine AL, Del Valle HB, eds. *Dietary Reference Intakes for Calcium and Vitamin D*. Washington, DC: National Academies Press, 2011.

TABLE 21-9

**FIBER REQUIREMENTS: ADEQUATE INTAKE\***

Age	Total Fiber (g/day)
0–12 mo	Not determined
1–3 yr	19
4–8 yr	25
9–13 yr, boys	31
9–13 yr, girls	26
14–18 yr, boys	38
14–18 yr, girls	26
Pregnancy	28
Lactation	29

\*Adequate intake (AI). If sufficient scientific evidence unavailable to establish recommended dietary allowance (RDA), an AI is usually developed. For healthy breast-fed infants, the AI is the mean intake. AI for other life stage and gender groups is believed to cover the needs of all healthy individuals in the group, but a lack of data or uncertainty in the data prevents being able to specify with confidence the percentage of individuals covered by this intake.

Modified from Otten JJ, Hellwig JP, Meyers LD, eds. *Dietary Reference Intakes: The Essential Guide to Nutrient Requirements*. Washington, DC: National Academies Press, 2006.

- b. Consider fluoride supplementation for those patients who use bottled water and home filtration systems. Most bottled water does not contain adequate amounts of fluoride. Some home water treatment systems can reduce fluoride levels.
- c. To avoid fluorosis, children should not use fluoridated toothpaste until age 2 years, and then only a small pea-sized amount up to age 6 years. See Formulary for complete fluoride recommendations (i.e., in areas where water is not fluoridated).

## F. Fiber Requirements (Table 21-9)<sup>7</sup>

## V. ENTERAL NUTRITION

### A. Mixing Instructions for Full-Term Standard and Soy-Based Infant Formulas (Table 21-10)

### B. Common Caloric Modulars

For the child who needs additional protein, carbohydrate, fat, or a combination (Table 21-11)

### C. Enteral Formulas, Including Their Main Nutrient Components (Table 21-12)

A comprehensive (but not complete) list. Most of these formulas are cow's milk-based and designed for normal digestive tracts.

### D. Clinical Conditions Requiring Special Diets, and Suggested Formula(s) (Table 21-13)

A comprehensive (but not complete) list of special clinical conditions (e.g., cow's milk allergy or intolerance) and the growing number of formulas designed for these conditions.

### E. Common Oral Rehydration Solutions (Table 21-14)

TABLE 21-10

## PREPARATION OF INFANT FORMULAS FOR FULL-TERM STANDARD AND SOY FORMULAS\*

Formula Type	Caloric Concentration (kcal/oz)	Amount of Formula	Water (oz)
Liquid concentrates (40 kcal/oz)	20	13 oz	13 oz
	24	13 oz	8.5 oz
	27	13 oz	6.3 oz
	30	13 oz	4.3 oz
Powder (44 kcal/scoop)	20	1 scoop	2 oz
	24	3 scoops	5 oz
	27	3 scoops	4.25 oz
	30	3 scoops	4 oz

\*Does not apply to Enfacare, Neocate Infant, Neosure. Enfamil AR should not be concentrated greater than 24 kcal/oz. Use a packed measure for Nutramigen LIPIL and Pregestimil LIPIL; all others unpacked powder.

TABLE 21-11

## COMMON CALORIC MODULARS\*

Component	Calories
<b>PROTEIN</b>	
Beneprotein (powder)	25 kcal/scoop (6 g protein)
Prosource protein powder	30 kcal/scoop (6 g protein)
Complete Amino Acid Mix	3.28 kcal/g (0.82 g protein)
Liquid Protein Fortifier	0.67 kcal/mL (0.167 g protein/mL)
<b>CARBOHYDRATE</b>	
Polycose	Powder: 3.8 kcal/g
SolCarb	3.75 kcal/g; 15 kcal/tablespoon
<b>FAT</b>	
MCT oil†	7.7 kcal/mL
Vegetable oil	8.3 kcal/mL
Microlipid	4.5 kcal/mL
Liquigen (emulsified MCT)	4.5 kcal/mL
<b>FAT AND CARBOHYDRATE</b>	
Duocal	42 kcal/15 mL; 25 kcal/scoop (59% Carb, 41% Fat, 35% fat as MCT)

\*Use these caloric supplements when you want to increase protein or when you have reached the maximum concentration tolerated and wish to further increase caloric density.

†Medium-chain triglyceride (MCT) oil is unnecessary unless there is fat malabsorption.

TABLE 21-12

## ENTERAL NUTRITION COMPONENTS (PER LITER)

## A. INFANT FORMULAS

	Kcal/oz	Protein (g)	Fat (g)	Carbs (g)	Na (mEq)	K (mEq)	Ca (mg)	P (mg)	Fe (mg)	Osmolality
<b>HUMAN MILK</b>										
Term	20	11	39	72	8	14	279	143	0.3	286
Preterm	20	14	39	66	11	15	248	128	1.2	290
<b>HUMAN MILK AND FORTIFIERS ANALYSIS</b>										
Enfamil HMF Liquid + Preterm Human Milk (5 mL + 25 mL breastmilk)	24	32	48	65	20	20	1100	640	15	322
Similac HMF + Preterm Human Milk (1 pkt/25 mL)	24	23	41	82	17	30	1381	777	4.6	N/A
<b>PRETERM FORMULAS</b>										
Enfamil Enfacare	22	21	39	77	11	20	890	490	13.3	260
Enfamil Premature 20	20	20	34	74	17	17	1100	553	3.4	240
Enfamil Premature 24 High Protein	24	28	41	85	20	21	1340	670	15	300
Enfamil Premature 30	30	30	52	112	26	28	1670	840	18	300
Gerber Good Start Premature 20	20	20	35	71	16	21	1110	570	12	229
Gerber Good Start Premature 24 High Protein	24	29	42	78	19	25	1310	680	14	299
Gerber Good Start Premature 30	30	30	53	107	24	31	1660	860	18	341
Gerber Good Start Nourish	22	21	38	76	12	20	880	470	13	275
Similac Neosure	22	21	41	75	11	27	781	461	13.4	250
Similac Special Care 20	20	20	37	70	13	22	1217	676	12.2	235
Similac Special Care 24 High Protein	24	27	44	81	15	27	1461	811	14.6	280
Similac Special Care 30	30	30	67	78	19	34	1826	1014	18.3	325

Continued

TABLE 21-12

## ENTERAL NUTRITION COMPONENTS (PER LITER) (Continued)

A. INFANT FORMULAS (Continued)	Kcal/oz	Protein (g)	Fat (g)	Carbs (g)	Na (mEq)	K (mEq)	Ca (mg)	P (mg)	Fe (mg)	Osmolality
<b>COW'S MILK-BASED FORMULAS</b>										
Enfamil Infant	20	14	36	74	8	19	520	287	12	300
Enfamil Newborn	20	14	36	73	8	19	520	287	12	300
Enfamil A.R.	20	17	34	74	12	19	520	353	12	230 (240*)
Enfamil LactoFree	20	14	36	73	9	19	547	307	12	200
Enfagrow Toddler Transitions	20	18	36	70	10	23	1300	867	13.4	270
Evap. Milk (13 oz + 19 oz water + 30 mL corn syrup)	20	27	31	72	21	32	1066	832	0.8	N/A
Organic Milk-Based Infant Formula	20	15	36	71	7	15	420	280	12	294
Parent's Choice Premium Infant Formula	20	14	36	72	8	19	520	287	12	295
Similac Advance	20	14	37	76	7	18	528	284	12	310
Similac Go and Grow Milk-Based Formula	20	14	37	72	7	18	1014	548	13.5	300
Similac Sensitive	20	14	37	72	9	19	568	379	12.2	200
Similac Advance Organic	20	14	37	71	7	18	528	284	12.2	225
Similac PM 60/40	20	15	38	69	7	14	379	189	4.7	280
Similac for Spitup	20	14	37	72	9	19	568	379	12.2	180
<b>SOY-BASED</b>										
America's Store Brand Soy (also w/ARA/DHA)	20	17	36	68	11	21	700	460	12	164
Enfamil Prosobee	20	17	36	71	11	21	700	460	12	170
Enfagrow Soy Next Step	20	22	30	79	11	21	1300	867	13.3	230
Gerber Good Start Soy	20	17	34	75	12	20	704	422	12.1	180
Gerber Good Start 2 Soy	20	19	34	73	12	20	1273	710	13.4	175

Similac Soy Isomil	20	17	37	70	13	19	710	507	12.2	200
Similac for Diarrhea	20	18	37	68	13	19	710	507	12.2	240
Similac Go and Grow Soy-Based Formula	20	17	37	70	13	19	1014	676	13.5	200
<b>CASEIN, EXTENSIVELY HYDROLYZED</b>										
Alimentum	20	19	37	69	13	20	710	507	12.2	370
Nutramigen	20	19	36	69	14	19	627	347	12	300 (320*)
Nutramigen with Enflora LGG	20	19	36	69	14	19	627	347	12	300
Pregestimil	20	19	38	69	14	19	640	350	12.2	250
<b>WHEY, PARTIALLY HYDROLYZED</b>										
Gerber Good Start Gentle	20	15	34	78	8	19	449	255	10.1	250
Gerber Good Start Protect	20	15	34	75	8	19	449	255	10.1	250
Gerber Good Start 2 Gentle	20	15	34	78	8	19	1273	710	13.4	180
Gerber Good Start 2 Protect	20	15	34	75	8	19	1273	710	13.4	180
Gerber Good Start Soothe	20	15	34	75	8	19	480	270	10	195
<b>WHEY AND CASEIN, PARTIALLY HYDROLYZED</b>										
Enfamil Gentlease	20	15	36	72	10	19	547	307	12	230
<b>AMINO ACID-BASED</b>										
Elecare Infant	20	20	32	72	13	26	780	568	10	350
Neocate Infant	20	21	30	78	11	27	830	624	12.4	375
PurAmino	20	19	36	69	14	19	627	347	12	350
<b>SPECIALIZED</b>										
3232A	20	19	28	89	13	19	627	420	12.5	250
RCF	20	20	36	68	13	19	710	507	12.2	168
Enfaport	30	35	54	102	13	29	940	520	18	280

Continued



TABLE 21-12

## ENTERAL NUTRITION COMPONENTS (PER LITER) (Continued)

B. TODDLER AND YOUNG CHILD 1–10 YEARS (Continued)										
	Kcal/oz	Protein (g)	Fat (g)	Carbs (g)	Na (mEq)	K (mEq)	Ca (mg)	P (mg)	Fe (mg)	Osmolality
B. TODDLER AND YOUNG CHILD 1–10 YEARS										
COW'S MILK–BASED FORMULAS										
Boost Kid Essentials	30	30	38	135	24	30	1181	886	14	550/600/570
Boost Kid Essentials 1.5 (w/fiber)	45	42	75	165	30	33	1300	990	14	390 (405)
Carnation Instant Breakfast Essentials	24	43	16	105	24	27	1539	1539	13.8	N/A
Compleat Pediatric	30	38	39	132	33	42	1440	1000	14	380
Cow's Milk, 2%	15	35	20	50	22	41	1258	979	0.5	N/A
Cow's Milk, whole	19	34	34	48	22	40	1226	956	0.5	285
KetoCal 3 : 1	30	22	97	10	18	35	1140	801	16	180
KetoCal 4 : 1	43	30	144	6	26	55	1600	1300	22	197
Monogen	30	27	28	163	21	22	617	480	10.1	370
Nutren Junior (also w/fiber)	30	30	50	110	20	34	1000	800	14	350
Pediasure Enteral (also w/fiber)	30	30	40	133	17	34	972	845	14	335 (345)
Pediasure 1.5 (also w/fiber)	45	59	67	160 (165)	17	42	1476	1054	11	370 (390)
Pediasure Sidekicks	19	30	21	89	17	42	1055	844	11	420
Pediasure Sidekicks, Clear	18	30	0	120	8	4	175	750	9	325
Pediasure Vanilla	30	30	38	131	17	34	972	845	14	480
Pediasure with Fiber, Vanilla	30	30	38	135	17	34	972	845	14	480
Portagen	30	32	44	104	22	29	850	642	17	350
SOY-BASED										
Bright Beginnings Soy Pediatric Drink	30	30	50	109	17	40	970	800	14	350

**SEMI-ELEMENTAL, HYDROLYZED**

Peptamen Junior Fiber	30	30	39	137	20	34	1000	800	14	390
Peptamen Junior with Prebio	30	30	39	137	20	34	1000	800	14	365
Peptamen Junior, unflavored (w/fiber, vanilla flavored)	30	30	39	138	20	34	1000	800	14	260 (390)
Peptamen Junior 1.5	45	45	68	180	30	51	1652	1352	20.8	450
Pediasure Peptide (also flavored)	30	30	41	134	31	35	1060	844	14	250 (390)
Pediasure Peptide 1.5	45	45	61	201	47	52	1580	1265	21	450

**SOY AND PORK, HYDROLYZED**

Pepdite Junior, Unflavored	30	31	50	106	18	35	1130	940	14	430
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**AMINO ACID-BASED**

Elecare Jr, Unflavored and Vanilla	30	31	49	109	20	39	1172	852	15	560
E028 Splash	30	25	35	146	9	24	620	620	7.7	820
Neocate Junior Flavored	30	35	47	110	19	36	1200	738	16	690
Neocate Junior Unflavored	30	33	50	104	18	35	1130	697	15	590
Vivonex Pediatric	24	24	24	130	17	31	970	800	10	360

**C. OLDER CHILDREN AND ADULT STANDARD FORMULAS**

	Kcal/oz	Protein (g)	Fat (g)	Carbs (g)	Na (mEq)	K (mEq)	Ca (mg)	P (mg)	Fe (mg)	Osmolality
<b>COW'S MILK-BASED FORMULAS</b>										
Boost	30	40	17	171	24	43	1250	1250	19	625
Boost Glucose Control	32	59	50	84	48	29	1160	928	15	400
Boost High Protein	30	63	25	138	31	41	1459	1250	19	650
Boost Plus	45	59	59	188	31	41	1,459	1250	19	670
Compleat	32	48	40	128	43	44	760	760	14	340
Ensure Clear	30	35	0	215	8	0	0	0	9	700
Ensure Immune Health	32	38	25	177	37	40	1266	1055	19	620

TABLE 21-12

## ENTERAL NUTRITION COMPONENTS (PER LITER) (Continued)

C. OLDER CHILDREN AND ADULT STANDARD FORMULAS (Continued)										
	Kcal/oz	Protein (g)	Fat (g)	Carbs (g)	Na (mEq)	K (mEq)	Ca (mg)	P (mg)	Fe (mg)	Osmolality
Ensure Plus	45	55	212	47	41	45	1266	1266	19	680
Glucerna 1.0 Cal	30	42	54	96	41	40	705	705	13	355
Jevity 1 Cal	32	44	35	155	40	40	910	760	14	300
Jevity 1.2 Cal	36	56	39	169	59	47	1200	1200	18	450
Jevity 1.5 Cal	45	64	50	216	61	55	1200	1200	18	525
Nepro	54	81	96	167	46	27	1060	700	19	585
Novasource Renal	60	74	100	200	39	21	1300	650	18	700/960
Nutren 1.0, vanilla (w/fiber)	30	40	38	127	38	32	668	668	12	370 (410)
Nutren 1.5, unflavored	45	60	68	169	51	48	1000	1000	18	430
Nutren 2.0	60	80	104	196	57	49	1340	1340	24	745
Optimental	30	51	28	139	49	44	1055	1055	13	585
Osmolite 1 Cal	32	44	35	144	40	40	760	760	14	300
Osmolite 1.2 Cal	36	56	39	158	58	46	1200	1200	18	360
Osmolite 1.5 Cal	45	63	49	204	61	46	1000	1000	18	525
Promote (w/fiber)	30	63	26	130	44	51	1200	1200	18	340 (380)
Pulmocare	45	63	93	106	57	50	1060	1060	19	475
Renalcal	60	35	83	291	0	0	0	0	0	600
Replete, unflavored	30	63	34	113	39	39	1000	1000	18	300/350
Resource 2.0	60	84	88	217	35	39	1042	1042	18.8	790
Resource Breeze	32	38	0	230	15	1	42	633	11	750
Suplena	54	45	96	205	35	29	1055	717	19	600
TwoCal HN	60	84	91	219	64	63	1050	1050	19	725

<b>SOY-BASED</b>										
Fibersource HN	36	53	39	160	52	51	1000	1000	17	490
Isosource 1.5 CAL	45	68	65	170	56	58	1070	1070	19	650/585
Isosource HN	36	53	39	160	48	49	1200	1200	15	490
<b>SEMI-ELEMENTAL HYDROLYZED</b>										
Peptamen, unflavored	30	40	39	127	25	39	800	700	18	270
Peptamen with Prebio	30	40	39	127	25	39	800	700	18	300
Peptamen 1.5, unflavored	45	68	56	188	45	48	1000	1000	27	550
Peptamen AF	36	76	55	107	35	41	800	800	14.4	390
Peptamen Bariatric	30	93	38	78	29	34	670	670	12	345
Perative	39	67	37	180	45	44	870	870	16	460
Pivot 1.5	45	94	51	172	61	51	1000	1000	18	595
Vital 1.0 Cal	30	40	38	130	46	36	705	705	13	390
Vital HN	30	42	11	185	25	36	667	667	12	500
<b>AMINO ACID-BASED</b>										
Tolerex	30	21	1.5	230	20	30	560	560	10	550
Vivonex RTF	30	50	12	175	29	31	670	670	12	630
Vivonex Plus	30	45	7	190	27	27	560	560	10	650
Vivonex T.E.N.	30	38	3	210	26	24	500	500	9	630

\*Liquid formulation.

**TABLE 21-13****FORMULAS FOR SPECIAL CLINICAL CIRCUMSTANCES****A. INFANTS**

Preterm	
Pre-discharge	Enfamil Premature 20, 24 HP, 30 Similac Special Care Advance 20, 24 HP, 30 Gerber Good Start Premature 20, 24 HP, 30
Post-discharge (through 12 mo)	Enfamil Enficare Similac Neosure Gerber Good Start Nourish
Lactose intolerance	Enfamil LactoFree Similac Sensitive Similac for Diarrhea
Vegetarian, lactose intolerance, or galactosemia	America's Store Brand Soy Infant Formula Gerber Good Start Soy Gerber Good Start Soy 2 Similac Go and Grow Soy-Based Formula (9–24 mo) Similac Soy Isomil Enfagrow Soy NEXT STEP (9–24 mo) Enfamil Prosobee
Protein (e.g., cow's milk) allergy/intolerance and/or fat malabsorption	Alimentum Elecare Neocate Infant (and w/DHA and ARA) Nutramigen PurAmino Pregestimil
Severe carbohydrate intolerance	3232A RCF
Requiring lower calcium and phosphorus	Similac PM 60/40

**B. TODDLERS AND YOUNG CHILDREN AGES 1–10 YR**

Vegetarian, lactose intolerance, or milk protein intolerance	Bright Beginnings Soy Pediatric Drink
Protein allergy/intolerance and/or fat malabsorption	Pediasure Peptide (and 1.5) Pepdite Jr Peptamen Jr (with and without Prebio) Vivonex Pediatric Elecare Jr Neocate Junior (Unflavored and Flavored) EO28 Splash
Fat malabsorption, intestinal lymphatic obstruction, chylothorax	Portagen Monogen Enfaport
Increased caloric needs	Boost Kids Essentials Carnation Instant Breakfast Essentials Nutren Junior (also with fiber) Pediasure (also with fiber)
Requiring clear liquid diet	Resource Breeze Ensure Clear Pediasure Sidekicks Clear

TABLE 21-13

**FORMULAS FOR SPECIAL CLINICAL CIRCUMSTANCES (Continued)**

Intractable epilepsy	KetoCal (3:1 and 4:1)
<b>C. OLDER CHILDREN AND ADULTS</b>	
Tube feeding	
For malabsorption of protein and/or fat	Peptamen, Peptamen w/ Prebio, Peptamen 1.5 Perative Tolerex Vital HN Vital 1.0 Cal Vivonex Plus and Vivonex T.E.N
For critically ill and/or malabsorption	Optimental Pulmocare Pivot 1.5 Perative
For impaired glucose tolerance	Glucerna Glytrol Store Brand Diabetic Nutritional Drink
For dialysis patients	Magnacal Renal Nepro NutriRenal
For patients with acute renal failure not on dialysis	Renalcal Suplena
Increased caloric needs (oral)	
With a normal gastrointestinal (GI) tract	Boost, Boost with fiber Boost Plus, Boost High Protein Carnation Instant Breakfast Essentials with whole milk Ensure NUTRA Shake
For clear liquid diet	Resource Breeze Ensure Clear Pediasure Sidekicks Clear
For patients with cystic fibrosis (CF)	Scandishake with whole milk

TABLE 21-14

**ORAL REHYDRATION SOLUTIONS**

Solution	Kcal/mL (kcal/oz)	Carbohydrate (g/L)	Na (mEq/L)	K (mEq/L)	Osmolality (mOsm/kg H <sub>2</sub> O)
CeraLyte-70	0.16 (4.9)	Rice digest (40)	70	20	N/A
CeraLyte-50	0.16 (4.9)	Rice digest (40)	50	20	N/A
CeraLyte-90	0.16 (4.9)	Rice digest (40)	90	20	N/A
Enfalyte	0.12 (3.7)	Rice syrup solids (30)	50	25	170
Oral Rehydration Salts (WHO)	0.06 (2)	Dextrose (20)	90	20	330
Pedialyte (unflavored)	0.1 (3)	Dextrose (25)	45	20	250

## VI. PARENTERAL NUTRITION <sup>12</sup>

Necessary to adequately support the pediatric patient with insufficient enteral intake.

### A. Situations Where Parenteral Nutrition(PN) is Suggested

1. **Inability to feed enterally** (e.g., extreme prematurity, tracheoesophageal fistulas)
2. **When alimentation via gastrointestinal tract has to be restricted for >5 days** (e.g., chylothorax/chylous ascites, bowel pseudo-obstruction)
3. **Gastrointestinal (GI) dysfunction and/or malabsorption** (e.g., short gut syndrome, intestinal atresias, enteric fistulas, gastroschisis)
4. **Increased losses or requirements** (e.g., severe diarrhea, intractable vomiting, persistent or severe failure to thrive)

### B. Suggested Formulations for Initiation and Advancement of PN (Table 21-15)

Suggested glucose, protein, and fat during initiation, as well as recommendations for advancement and maximum allowable amounts

### C. Recommended Parenteral Formulations (Table 21-16)

Based on age groups; includes recommendations for electrolytes, elements, and minerals

### D. Suggested Monitoring Schedule for Patients Receiving Parenteral Nutrition (Table 21-17)

Important to monitor growth parameters, as well as laboratory studies for these patients on periodic basis

TABLE 21-15

#### INITIATION AND ADVANCEMENT OF PARENTERAL NUTRITION\*

Nutrient	Initial Dose	Advancement	Maximum
Glucose	5%–10%	2.5%–5%/day	12.5% peripheral 18 mg/kg/min (maximum rate of infusion)
Protein	1–1.5 g/kg/day	0.5–1 g/kg/day	3–4 g/kg/day 10%–16% of calories
Fat†	0.5–1 g/kg/day	1 g/kg/day	4 g/kg/day 0.17 g/kg/hr (maximum rate of infusion)

\*Acceptable osmolality of parenteral nutrition through a peripheral line varies between 900 and 1050 osm/L by institution. An estimate of the osmolality of parenteral nutrition can be obtained with the following formula: Estimated osmolality = (dextrose concentration × 50) + (amino acid concentration × 100) + (mEq of electrolytes × 2). Consult individual pharmacy for hospital limitations.

†Essential fatty acid deficiency (EFAD) may occur in fat-free parenteral nutrition within 2–4 weeks in infants and children and as early as 2–14 days in neonates. A minimum of 2%–4% of total caloric intake as linoleic acid and 0.25%–0.5% as linolenic acid is necessary to meet essential fatty acid requirements.

Modified from Baker RD, Baker SS, Davis AM. *Pediatric Parenteral Nutrition*. New York: Chapman and Hall, 1997; and Cox JH, Melbardis IM. Parenteral nutrition. In: Samour PQ, King K, eds. *Handbook of Pediatric Nutrition*. 3rd ed. Boston: Jones and Bartlett Publishers, 2005.

TABLE 21-16

## PARENTERAL NUTRITION FORMULATION RECOMMENDATIONS

Component	Preterm	Term				
		Infants	1–3 yr	4–6 yr	7–10 yr	11–18 yr
Energy (kcal/kg/day)	85–105	90–108	75–90	65–80	55–70	30–55
Protein (g/kg/day)	2.5–4	2.5–3.5	1.5–2.5	1.5–2.5	1.5–2.5	0.8–2
Sodium (mEq/kg/day)	2–4	2–4	2–4	2–4	2–4	60–150 mEq/day
Potassium (mEq/kg/day)	2–4	2–4	2–4	2–4	2–4	70–180 mEq/day
Calcium (mg/kg/day)	50–60	20–40	10–20	10–20	10–20	200–800 mg/day
Phosphorus (mg/kg/day)	30–45	30–45	15–40	15–40	15–40	280–900 mg/day
Magnesium (mEq/kg/day)	0.5–1	0.25–1	0.25–0.5	0.25–0.5	0.25–0.5	8–24 mEq/day
Zinc (mcg/kg/day)	325–400	100–250	100	100	50	2–5 mg/day
Copper (mcg/kg/day)*	20	20	20	20	5–20	200–300 mcg/day
Manganese (mcg/kg/day)*	1	1	1	1	1	40–50 mcg/day
Selenium (mcg/kg/day)	2	2	2	2	1–2	40–60 mcg/day

\*Copper and manganese needs may be lowered in cholestasis.

Modified from Baker RD, Baker SS, Davis AM. *Pediatric Parenteral Nutrition*. New York: Chapman and Hall, 1997; Cox JH, Melbardis IM. Parenteral nutrition. In: Samour PQ, King K, eds. *Handbook of Pediatric Nutrition*. 3rd ed. Boston: Jones and Bartlett Publishers, 2005; and American Society for Parenteral and Enteral Nutrition (ASPEN). Safe practices for parenteral nutrition. *JPEN J Parenter Enteral Nutr*. 2004;28(6):S39–S70.

TABLE 21-17

## MONITORING SCHEDULE FOR PATIENTS RECEIVING PARENTERAL NUTRITION\*

Variable	Initial Period <sup>†</sup>	Later Period <sup>‡</sup>
<b>GROWTH</b>		
Weight	Daily	2 times/wk
Height	Weekly (infants)	
	Monthly (children)	Monthly
Head circumference (infants)	Weekly	Monthly <sup>§</sup>
<b>LABORATORY STUDIES</b>		
Electrolytes and glucose	Daily until stable	Weekly
BUN/creatinine	Twice weekly	Weekly
Albumin or prealbumin	Weekly	Weekly
Ca <sup>2+</sup> , Mg <sup>2+</sup> , P	Twice weekly	Weekly
ALT, AST, ALP	Weekly	Weekly
Total and direct bilirubin	Weekly	Weekly
CBC	Weekly	Weekly
Triglycerides	With each increase	Weekly
Vitamins	—	As indicated
Trace minerals	—	As indicated

\*For patients on long-term parenteral nutrition, monitoring every 2–4 weeks is adequate in most cases.

<sup>†</sup>The period before nutritional goals are reached or during any period of instability.

<sup>‡</sup>When stability is reached, no changes in nutrient composition.

<sup>§</sup>Weekly in preterm infants.

ALP, Alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase; BUN, blood urea nitrogen; CBC, complete blood cell count.



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# Chapter 22

## Oncology

M. Eric Kohler, MD, PhD

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 See additional content on Expert Consult

### I. WEBSITES

National Cancer Institute (NCI): <http://www.cancer.gov/cancertopics/pdq/pediatrictreatment>

SEER (Surveillance, Epidemiology, and End Results) data from the NCI: <http://seer.cancer.gov/>

Long-term follow-up guidelines for survivors of pediatric cancer: <http://www.survivorshipguidelines.org/>

National Cancer Institute Clinical Trial Database: [www.cancer.gov/clinicaltrials](http://www.cancer.gov/clinicaltrials)

### II. PRESENTING SIGNS AND SYMPTOMS OF PEDIATRIC MALIGNANCIES (TABLE 22-1)

**NOTE:** Common presenting signs and symptoms of many malignancies include weight loss, failure to thrive, anorexia, malaise, fever, pallor, and lymphadenopathy.

TABLE 22-1

#### PRESENTING SIGNS AND SYMPTOMS OF PEDIATRIC MALIGNANCIES<sup>1,2</sup>

Malignancy	Signs and Symptoms	Initial Workup*	Incidence by Age
ALL	Anorexia, fatigue, malaise, irritability, low-grade fevers, bone pain/limp ± bone tenderness, bruising/bleeding, petechiae, hepatosplenomegaly, lymphadenopathy, painless testicular enlargement/mass	CBC with differential, peripheral blood smear, LDH, uric acid, electrolytes, including Ca and Phos	Peaks at age 2–5 years
AML	Similar to ALL; may also have subcutaneous nodules, gingival hyperplasia, chloromas (masses)	Same initial workup as ALL plus DIC testing	Peaks in first year of life, declines until age 4
Lymphoma	Painless lymphadenopathy, hepatosplenomegaly, stridor, cough, fever, weight loss, night sweats, fatigue, anorexia, pruritus, intussusception, focal neurologic symptoms, alcohol-induced pain	CBC with differential, peripheral smear, electrolytes including Ca and Phos, LFTs, ESR, ferritin, uric acid, LDH, CXR	HD peaks between 15 and 35 years of age; NHL peaks from age 5–19
Brain tumor	Headache, irritability, emesis, gait changes, focal neurologic symptoms, cranial nerve palsies, changes in vision, personality changes, diabetes insipidus, precocious puberty	MRI of brain and spine, ophthalmology examination, endocrine workup if pituitary dysfunction is suspected	Higher incidence in children <5 years

Continued

TABLE 22-1

PRESENTING SIGNS AND SYMPTOMS OF PEDIATRIC MALIGNANCIES (Continued)

Malignancy	Signs and Symptoms	Initial Workup*	Incidence by Age
Neuroblastoma	Abdominal mass, hepatomegaly, fever, irritability, bone pain, limp, subcutaneous nodules, SVC syndrome, Horner syndrome, peri-orbital ecchymoses, opsoclonus-myoclonus, secretory diarrhea	Abdominal ultrasound, CT chest/abdomen/pelvis, urine HVA and VMA	Peaks at <2 years of age
Wilms tumor	Abdominal mass, abdominal pain, hypertension, hematuria	Abdominal ultrasound, abdominal CT or MRI, urinalysis, CBC	Peaks at age 2–5
Bone sarcoma	Long-bone pain not relieved with conservative treatment; limp, swelling, fracture	X-ray of primary site, CT of chest	Peaks at age 10–20
Rhabdomyosarcoma	Localized symptoms based on location of tumor; painful or painless mass, proptosis, hearing loss, urinary obstruction, hematuria	CT or MRI of primary site	Peaks at <6 years of age and in adolescence
Retinoblastoma	Leukocoria, strabismus, hyphema, irregular pupil(s)	Ophthalmology referral	Peaks at age 2
Hepatoblastoma	Abdominal mass, anorexia, emesis, abdominal pain, fever	CBC, LFTs, AFP, hepatitis B and C titers, abdominal ultrasound	Peaks at <3 years of age
Histiocytic disease	Scaly papular rash, fever, weight loss, gingival hyperplasia, diarrhea, pituitary dysfunction, precocious puberty, polydipsia, polyuria, long-bone pain	Skeletal survey, CXR, CBC, LFTs, LDH, ferritin, uric acid, triglycerides, urine osmolality, skin biopsy	Variable
Gonadal tumor	Testicular masses, scrotal swelling. Ovarian tumors are typically asymptomatic until quite large	Ultrasound, CT or MRI, AFP, $\beta$ -hCG, LDH	Peaks in adolescence

\*Laboratory test and imaging suggestions are meant as a guide for evaluation of a potential malignancy. Patients warranting definitive testing should be referred to an oncologist.

AFP,  $\alpha$ -Fetoprotein; ALL, acute lymphocytic leukemia; AML, acute myeloid leukemia;  $\beta$ -hCG, beta human chorionic gonadotropin; Ca, calcium; CBC, complete blood cell count; CT, computed tomography; CXR, chest x-ray; DIC, disseminated intravascular coagulation; ESR, erythrocyte sedimentation rate; HD, Hodgkin disease; HVA/VMA, homovanillic acid/vanillylmandelic acid (urine catecholamines); LDH, lactate dehydrogenase; LFTs, liver function tests; MRI, magnetic resonance imaging; NHL, non-Hodgkin lymphoma; Phos, phosphorus; SVC, superior vena cava.

### III. EVALUATION OF LYMPHADENOPATHY

#### A. Etiology

- Reactive lymph node (LN):** Majority of lymphadenopathy
- Direct infection of LN:** Suppurative lymphadenitis (typically due to *Staphylococcus* or *Streptococcus*) or indolent lymphadenitis (e.g., *Bartonella*, atypical *Mycobacterium* [tuberculosis])

3. **Malignancy:** Can be seen in leukemias, lymphomas, and some solid tumors. Less common than infectious causes
4. **Other causes:** Autoimmune disorders, drug reactions, serum sickness, hypothyroidism, and sarcoidosis

## B. Physical Findings

1. **Size:** Cervical and axillary LN are typically <1 cm in size. Inguinal LN are typically <1.5 cm in size. Cervical LN >2 cm or palpable supraclavicular LN are associated with higher risk for malignancy.
2. **Palpation:** Tenderness is more common with reactive or infected LN but does not exclude malignancy. Fluctuance, warmth, and/or overlying erythema are more common in lymphadenitis. Hard, rubbery, fixed, or matted LN are suspicious for malignancy and require further investigation.

## C. Initial Workup

1. **If reactive lymphadenopathy is suspected,** consider observation, with expected decrease in size over 4–6 weeks and resolution in 8–12 weeks.
2. **If lymphadenitis is suspected,** consider a 10–14 day trial of antibiotics with streptococcal and staphylococcal coverage.
3. **Laboratory studies:** Complete blood cell count (CBC) with differential, erythrocyte sedimentation rate (ESR), lactate dehydrogenase (LDH), specific serologies based on exposures and symptoms (*Bartonella*, Epstein-Barr virus [EBV], human immunodeficiency virus [HIV]), tuberculin skin testing, chest x-ray.

## IV. COMMONLY USED CHEMOTHERAPEUTIC DRUGS AND ASSOCIATED ACUTE TOXICITIES (TABLE 22-2)

TABLE 22-2

### CHARACTERISTICS OF CHEMOTHERAPEUTIC AGENTS

Drug Name ( <i>Drug Class</i> )	Toxicity*
Asparaginase (L-Asp, PEG-Asp, Elspar, <i>Erwinia</i> ) ( <i>Enzyme</i> )	DLT: pancreatitis, seizures, hypersensitivity reactions (both acute and delayed; less with PEG-modified), encephalopathy Other: nausea, pancreatitis, hyperglycemia, azotemia, fever, coagulopathy, sagittal sinus thrombosis and other venous thromboses, hyperammonemia Long-term: stroke
Bevacizumab (Avastin) ( <i>VEGF inhibitor</i> )	DLT: wound healing, hemorrhage, thromboembolic events, CHF Other: abdominal pain, constipation, mucositis, dizziness, headache, dyspnea, epistaxis
Bleomycin (Blenoxane) ( <i>DNA strand breaker</i> )	DLT: anaphylaxis, pneumonitis Other: pain, fever, chills, mucositis, skin reactions Long-term: pulmonary fibrosis
Busulfan (Myleran) ( <i>Alkylator</i> )	DLT: myelosuppression, mucositis, seizures, veno-occlusive disease Other: hyperpigmentation, hypotension Long-term: infertility, endocardial fibrosis, secondary malignancy

Continued

TABLE 22-2

## CHARACTERISTICS OF CHEMOTHERAPEUTIC AGENTS (Continued)

Drug Name ( <i>Drug Class</i> )	Toxicity*
Carboplatin (CBDCA, Paraplatin) ( <i>DNA cross-linker</i> )	DLT: thrombocytopenia, nephrotoxicity Other: severe emesis, ototoxicity, peripheral neuropathy, optic neuritis (rare) Long-term: renal insufficiency, hearing loss
Carmustine (bischloronitrosourea, BCNU, BiCNU) ( <i>Alkylator</i> )	DLT: myelosuppression (prolonged cumulative) Other: vesicant; brownish discoloration of skin, hepatic and renal toxicity, severe emesis Long-term: pulmonary fibrosis, infertility, secondary malignancy
Cisplatin ( <i>cis</i> -platinum, CDDP, Platinol) ( <i>DNA cross-linker</i> )	DLT: tubular and glomerular nephrotoxicity (related to cumulative dose), peripheral neuropathy, severe emesis Other: myelosuppression, ototoxicity, SIADH (rare), papilledema and retrobulbar neuritis (rare) Long-term: renal insufficiency, hearing loss, peripheral neuropathy
Cladribine (2-CdA, Leustatin) ( <i>Nucleotide analog</i> )	Myelosuppression, nausea and vomiting, headache, fever, chills, fatigue
Clofarabine (Clolar) ( <i>Purine analog</i> )	Capillary leak syndrome, veno-occlusive disease, increased creatinine, hyperbilirubinemia
Cyclophosphamide (CTX, Cytoxan) ( <i>Alkylator prodrug</i> )	DLT: leukopenia, cardiomyopathy Other: hemorrhagic cystitis (improved by mesna), emesis, direct ADH effect, SIADH Long-term: infertility, cardiomyopathy, secondary malignancy, leukoencephalopathy
Cytarabine (Ara-C) ( <i>Nucleotide analog</i> )	DLT: myelosuppression, cerebellar toxicity Other: rash, fever, conjunctivitis, nausea and vomiting, anorexia, diarrhea, metallic taste, severe GI ulceration, lethargy, ataxia, nystagmus, slurred speech, respiratory distress rapidly progressing to pulmonary edema, influenza-like syndrome
Dacarbazine (DIC, DTIC, imidazole carboxamide, DTIC-Dome) ( <i>Alkylator</i> )	DLT: myelosuppression Other: severe emesis, transaminitis, facial paresthesias (rare), rash Long-term: infertility
Dactinomycin (actinomycin D) ( <i>Antibiotic</i> )	DLT: myelosuppression, severe diarrhea Other: vesicant; nausea, acne, erythema, radiation recall, veno-occlusive disease Long-term: secondary malignancy
Daunorubicin (daunomycin) ( <i>Anthracycline</i> )	DLT: leukopenia, arrhythmia, congestive heart failure (related to cumulative dose) Other: stomatitis, emesis, vesicant, red urine, radiation recall Long-term: cardiomyopathy
Doxorubicin (Adriamycin) ( <i>Anthracycline</i> )	Refer to daunorubicin
Etoposide (VP-16, VePesid) ( <i>Topoisomerase inhibitor</i> )	DLT: leukopenia, anaphylaxis (rare), transient cortical blindness Other: hyperbilirubinemia, transaminitis, peripheral neuropathy (rare), hypotension Long-term: secondary malignancy (AML)
Fludarabine (Fludara) ( <i>Nucleotide analog</i> )	Myelosuppression, anorexia, increased AST, somnolence, fatigue Long-term: peripheral neuropathy, immunosuppression

TABLE 22-2

## CHARACTERISTICS OF CHEMOTHERAPEUTIC AGENTS (Continued)

Drug Name ( <i>Drug Class</i> )	Toxicity*
Fluorouracil (5-FU, Adrucil) ( <i>Nucleotide analog</i> )	DLT: myelosuppression, mucositis, severe diarrhea Other: hand-foot syndrome, tear duct stenosis, hyperpigmentation, loss of nails, cerebellar syndrome (rare), anaphylaxis
Gemcitabine ( <i>Pyrimidine analog</i> )	Peripheral edema, rash, nausea, vomiting, constipation, transaminase elevation, myalgias, neuropathy, HUS, pulmonary edema
Hydroxyurea (Hydrea) ( <i>Ribonucleotide reductase inhibitor</i> )	DLT: leukopenia, pulmonary edema (rare) Other: megaloblastic erythropoiesis, hyperpigmentation, azotemia, transaminitis, radiation recall
Idarubicin (idarubicin) ( <i>Anthracycline</i> )	DLT: arrhythmia, cardiomyopathy (cumulative) Other: vesicant; diarrhea, mucositis, enterocolitis Long-term: cardiomyopathy
Ifosfamide (isophosphamide, Ifex) ( <i>Alkylator prodrug</i> )	DLT: myelosuppression, mental status changes, dizziness, encephalopathy (rarely progressing to death), renal tubular damage Other: emesis, hemorrhagic cystitis (improved with mesna), direct ADH effect, SIADH, Fanconi syndrome Long-term: secondary malignancy, infertility
Irinotecan (Camptosar, IRN) ( <i>Topoisomerase I inhibitor</i> )	DLT: diarrhea Other: nausea and vomiting, asthenia, hyperbilirubinemia, dizziness, cough, dyspnea
Imatinib (Gleevec) ( <i>Tyrosine kinase inhibitor</i> )	CHF, edema, pleural effusion, rash, night sweats, weight gain, myalgias, fever
Lomustine (CCNU) ( <i>Alkylating agent</i> )	Myelosuppression, nausea and vomiting, disorientation, fatigue Long-term: secondary malignancy (leukemia)
Mechlorethamine (nitrogen mustard, HN <sub>2</sub> [mustine], Mustargen) ( <i>Alkylator</i> )	DLT: leukopenia, thrombocytopenia Other: severe emesis; vesicant; peptic ulcer (rare) Long-term: secondary malignancy, infertility
Melphalan (L-PAM, Alkeran) ( <i>Alkylator</i> )	DLT: prolonged leukopenia, mucositis, diarrhea Other: pruritus, emesis Long-term: pulmonary fibrosis, secondary malignancy, infertility, cataracts
Mercaptopurine (6-MP) ( <i>Nucleotide analog</i> )	DLT: hepatic necrosis and encephalopathy Other: headache, diarrhea, nausea Long-term: cirrhosis
Methotrexate (MTX, amethopterin, Folex, Mexate) ( <i>Folate antagonist</i> )	DLT: mucositis, diarrhea, renal dysfunction, encephalopathy, cortical blindness, ventriculitis (intrathecal) Other: photosensitivity, erythema, excessive lacrimation, transaminitis, pleuritis Long-term: leukoencephalopathy, cirrhosis, pulmonary fibrosis, aseptic necrosis of bone, osteoporosis
Mitoxantrone (dihydroxyanthracenedione dihydrochloride, Novantrone) ( <i>DNA intercalator</i> )	DLT: myelosuppression, cardiomyopathy Other: mucositis, blue-green urine Long-term: cardiomyopathy
Paclitaxel (Taxol) ( <i>Tubulin inhibitor</i> )	DLT: neutropenia, anaphylaxis, ventricular tachycardia and myocardial infarction (rare) Other: mucositis, peripheral neuropathy, bradycardia, hypertriglyceridemia

Continued

TABLE 22-2

## CHARACTERISTICS OF CHEMOTHERAPEUTIC AGENTS (Continued)

Drug Name ( <i>Drug Class</i> )	Toxicity*
Procarbazine (Matulane) ( <i>Alkylating agent</i> )	DLT: encephalopathy; pancytopenia, especially thrombocytopenia Other: emesis, paresthesias, dizziness, ataxia, hypotension; adverse effects with tyramine-rich foods, ethanol, MAOIs, meperidine, and many other drugs Long-term: secondary malignancy, infertility
Temozolomide (Temodar) ( <i>Alkylating agent</i> )	DLT: myelosuppression Other: constipation, headache, nausea, seizures
Teniposide (VM-26) ( <i>Topoisomerase inhibitor</i> )	DLT: leukopenia, anaphylaxis (rare) Other: hyperbilirubinemia, transaminitis Long-term: secondary malignancy (AML)
Thioguanine (6-TG, 6-thioguanine) ( <i>Nucleotide analog</i> )	DLT: myelosuppression, mucositis, diarrhea Other: hyperbilirubinemia, transaminitis, decreased vibratory sensation, ataxia, dermatitis
Thiotepa ( <i>Alkylating agent</i> )	DLT: cognitive impairment, leukopenia Other: increased AST, headache, dizziness, rash, desquamation Long-term: secondary malignancy (leukemia), impaired fertility, lower extremity weakness
Topotecan (Hycamptin) ( <i>Topoisomerase inhibitor</i> )	DLT: leukopenia, peripheral neuropathy (rare), Horner syndrome Other: nausea, diarrhea, transaminitis, headache
Vinblastine (BVL, vincaleukoblastine, Velban) ( <i>Microtubule inhibitor</i> )	DLT: leukopenia Other: vesicant; constipation, bone pain (especially in the jaw), peripheral and autonomic neuropathy, SIADH (rare)
Vincristine (VCR, Oncovin) ( <i>Microtubule inhibitor</i> )	DLT: peripheral and autonomic neuropathy, constipation, jaw pain, encephalopathy, foot drop, ptosis Other: vesicant; bone pain, hoarseness, SIADH (rare), hyperbilirubinemia
Vinorelbine (Navelbine) ( <i>Microtubule inhibitor</i> )	Peripheral neuropathy, asthenia, hyperbilirubinemia, constipation, diarrhea, nausea, emesis
<b>CHEMOTHERAPY ADJUNCTS</b>	
Amifostine	Indication: reduces toxicity of radiation Side effects: hypotension (62%), nausea and vomiting, flushing, chills, dizziness, somnolence, hiccups, sneezing, hypocalcemia in susceptible patients (<1%), rigors (<1%), mild skin rash
Dexrazoxane	Indication: protective agent for anthracycline-induced cardiotoxicity Side effects: myelosuppression
Leucovorin	Indication: reduces methotrexate toxicity Side effects: allergic sensitization (rare)
Mesna	Indication: reduces risk of hemorrhagic cystitis Side effects: headache, limb pain, abdominal pain, diarrhea, rash

\*The dose-limiting toxicity (DLT) is the toxicity most likely to require adjustment or withholding of drug.

ADH, Antidiuretic hormone; AML, acute myeloid leukemia; AST, aspartate transaminase; CHF, congestive heart failure; GI, gastrointestinal; HUS, hemolytic uremic syndrome; MAOI, monoamine oxidase inhibitor; PEG, polyethylene glycol; SIADH, syndrome of inappropriate antidiuretic hormone; VEGF, vascular endothelial growth factor.

Modified from *Physician's Desk Reference*. 64th ed. Montvale, NJ: Medical Economics, 2010; Taketomo CK, Hodding JH, Kraus DM. *American Pharmaceutical Association Pediatric Dosage Handbook*. 16th ed. Hudson OH: Lexi-Comp, 2009; and Micromedex 2.0: <http://www.thomsonhc.com/micromedex2/librarian>.

## V. ONCOLOGIC EMERGENCIES 4.5

## A. Hyperleukocytosis/Leukostasis

1. **Etiology:** Elevated white blood cell (WBC) count ( $\text{WBC} > 100,000/\mu\text{L}$ ) in leukemia patients, leading to leukostasis in the microcirculation and diminished tissue perfusion (notably in central nervous system [CNS] and lungs). This occurs more commonly and at lower WBC counts ( $>100,000/\mu\text{L}$ ) in acute myeloid leukemia (AML [especially M4 and M5]) than in acute lymphocytic leukemia (ALL [typically requiring a WBC count  $>300,000/\mu\text{L}$ ]). Leukostasis is very common in chronic myeloid leukemia (CML) but at WBC counts  $>300,000/\mu\text{L}$ .
2. **Presentation:** Hypoxia, tachypnea, and dyspnea from pulmonary leukostasis. Mental status changes, headaches, seizures, papilledema from cerebral leukostasis. Occasionally, gastrointestinal (GI) bleeding, abdominal pain, renal insufficiency, priapism, and intracranial hemorrhage. Leukostasis may be asymptomatic.
3. **Management:**
  - a. Transfuse platelets as needed to keep count above  $20,000/\mu\text{L}$ .
  - b. Avoid red blood cell (RBC) transfusions because they will raise viscosity (keep hemoglobin  $\leq 10$  g/dL). If RBCs are required, consider partial exchange transfusion.
  - c. Hydration, alkalinization, and allopurinol should be initiated (as discussed in Section V.B).
  - d. Administer fresh frozen plasma (FFP) and vitamin K for coagulopathy.
  - e. Before cytotoxic therapy, consider leukapheresis or exchange transfusion to lower WBC count if CNS or pulmonary symptoms exist.
  - f. Start disease treatment as soon as patient is clinically stable.

## B. Tumor Lysis Syndrome

1. **Etiology:** Lysis of tumor cells before or during early stages of chemotherapy (especially Burkitt lymphoma/leukemia, T-cell ALL).
2. **Presentation:** Hyperuricemia, hypocalcemia, hyperkalemia, hyperphosphatemia. Can lead to acute kidney injury due to precipitation of uric acid crystals and/or calcium phosphate crystals in renal tubules and microvasculature, respectively.
3. **Prevention and management:**
  - a. Hydration: Dextrose 5% ( $\text{D}_5$ ) 1/4 normal saline (NS)  $\pm 40$  mEq/L  $\text{NaHCO}_3$  (without K) at two times maintenance rate. Keep urine specific gravity  $<1.010$  and urine output  $>100\text{mL}/\text{m}^2/\text{hr}$ .
  - b. Hyperuricemia: Allopurinol inhibits formation of uric acid and can be given orally (PO) or intravenously (IV) (see Formulary for dosing). Rasburicase converts uric acid to the more soluble allantoin. Use in higher-risk patients, especially those with uric acid  $>7.5$  mg/dL.
  - c. Monitor  $\text{K}^+$ ,  $\text{Ca}^{2+}$ , phosphate, uric acid, and urinalysis closely (up to Q2 hr for high-risk patients). There is an increased risk of calcium phosphate precipitation when  $\text{Ca} \times \text{Phos} > 60$ .
  - d. Manage abnormal electrolytes as described in Chapter 11. See Chapter 19 for dialysis indications.



- e. Consider stopping alkalinization after uric acid levels return to normal to facilitate calcium phosphate excretion.

### C. Spinal Cord Compression

1. **Etiology:** Intrinsic or extrinsic compression of spinal cord; occurs most commonly with brain tumors, sarcomas, leukemia with lymphomatous involvement, lymphoma, and neuroblastoma.
2. **Presentation:** Back pain (localized or radicular), weakness, sensory loss, change in bowel or bladder function. Prognosis for recovery based on duration and level of disability at presentation.
3. **Diagnosis:** Magnetic resonance imaging (MRI [preferred]) or computed tomography (CT) scan of spine. A plain film of spine has good specificity but detects only two thirds of abnormalities.
4. **Management:** (**Note:** Steroids may prevent accurate diagnosis of leukemia/lymphoma; plan diagnostic procedure as soon as possible)
  - a. In the presence of neurologic abnormalities, strong history, and rapid progression of symptoms, immediately start bolus dexamethasone 1–2 mg/kg/day IV and obtain an emergent MRI of the spine.
  - b. With back pain but less acute symptoms and no anatomic level of dysfunction, consider lower dose of dexamethasone, 0.25–0.5 mg/kg/day PO, divided Q6 hr. Perform MRI of spine within 24 hours.
  - c. If cause of tumor is known, emergent radiotherapy or chemotherapy is indicated for sensitive tumors; otherwise, emergent neurosurgery consultation is warranted.
  - d. If cause of tumor is unknown or debulking may remove most or all of tumor, surgery is indicated to decompress the spine.

### D. Increased Intracranial Pressure

1. **Etiology:** Ventricular obstruction or impaired cerebrospinal fluid (CSF) flow.
2. **Presentation:** Headaches, irritability, lethargy, emesis (especially if projectile).
3. **Diagnosis:** Evaluate for vital sign changes (i.e., Cushing triad [ $\downarrow$  heart rate,  $\uparrow$  systolic blood pressure, irregular respirations]). Funduscopic evaluation for papilledema. Obtain CT or MRI of the head (MRI more sensitive for diagnosis of posterior fossa tumors).
4. **Management:**
  - a. See Chapter 4 for basic intracranial pressure (ICP) management.
  - b. If tumor is the cause, start IV dexamethasone: 1–2 mg/kg as first dose, then 0.5 mg/kg Q6 hr.
  - c. Obtain emergent neurosurgical consultation.
  - d. Consider mannitol for altered mental status and/or cardiovascular instability.

### E. Cerebrovascular Accident

1. **Etiology:** Hyperleukocytosis, coagulopathy, thrombocytopenia, radiation (fibrosis) or chemotherapy-related (e.g., L-asparaginase-induced hemorrhage or thrombosis, methotrexate). Most common in patients with leukemia.

## 2. **Diagnosis and management:**

- Platelet transfusions (and likely increase threshold for transfusion), FFP as needed to replace factors (e.g., if depleted by L-asparaginase)
- Brain CT with contrast, MRI, magnetic resonance angiography (MRA), or magnetic resonance venography (MRV) if venous thrombosis is suspected
- Administer heparin acutely, followed by warfarin, for thromboses (if no venous hemorrhage observed on MRI)
- Avoid L-asparaginase.
- Leukapheresis for hyperleukocytosis

## F. **Respiratory Distress and Superior Vena Cava Syndrome**

- Etiology:** Mediastinal mass, edema, or thrombosis; typically seen with Hodgkin disease, non-Hodgkin lymphoma (e.g., lymphoblastic lymphoma), ALL (T-lineage), germ cell tumors
- Presentation:** Orthopnea, headaches, facial swelling, dizziness, plethora, acute respiratory distress or failure
- Diagnosis:** Chest radiograph. Consider CT or MRI to assess airway. Attempt diagnosis of malignancy (if not known) by least invasive method possible. Avoid sedation or general anesthesia if unstable, high risk.
- Management:**
  - Control airway
  - Biopsy (e.g., bone marrow, pleurocentesis, lymphnode biopsy) before therapy if patient can tolerate sedation or general anesthesia
  - Empiric therapy: radiotherapy, steroids, chemotherapy

## G. **Typhilitis (Neutropenic Enterocolitis)**

- Etiology:** Inflammation of bowel wall, usually localized to cecum. Occurs most often in association with prolonged neutropenia.
- Presentation:** Right lower quadrant abdominal pain, nausea, diarrhea, fever (fever may be absent early in course; neutropenic patient with abdominal pain warrants evaluation for typhilitis and empirical antibacterial coverage). Risk for perforation.
- Diagnosis:**
  - Careful serial abdominal examinations
  - X-ray may show pneumatosis intestinalis, bowel wall edema
  - CT (IV and PO contrast) most sensitive imaging; may reveal bowel wall thickening, pneumatosis intestinalis
- Management:**
  - Nothing by mouth (NPO), IV fluids; consider nasogastric decompression.
  - Broad anaerobic and gram-negative antibiotic coverage (consider coverage for *Clostridium difficile*).
  - Follow closely with surgery consult.

## H. **Fever and Neutropenia**

- Etiology:** Presumed infection (bacterial, viral, or fungal) in a neutropenic host. Bacterial infection is the most common documented infection. Occasionally, fevers may be due to medications.

2. **Presentation:** Fever, fatigue, chills, rigors, listlessness, lethargy, tachypnea, tachycardia, localized pain.
3. **Diagnosis:** Fever (temperature [T]  $> 38.3^{\circ}\text{C}$  or  $T > 38.0^{\circ}\text{C}$  for  $>1$  hour) in the setting of neutropenia ( $\text{ANC} < 500$  cells/ $\mu\text{L}$ , or  $< 1000$  cells/ $\mu\text{L}$  but expected to drop to  $<500$  in the next 48 hours).
4. **Management:** See Fig. 22-1.

## VI. HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT)

### A. Goal

Administer healthy functioning hematopoietic stem cells from the bone marrow, peripheral blood, or umbilical cord blood to a patient whose bone marrow is diseased (from hematologic malignancy) or depleted (after treatment with myeloablative chemotherapy). HSCT is also used for some congenital and acquired hematologic, immunologic, and metabolic disorders.

### B. Types

#### 1. Allogeneic:

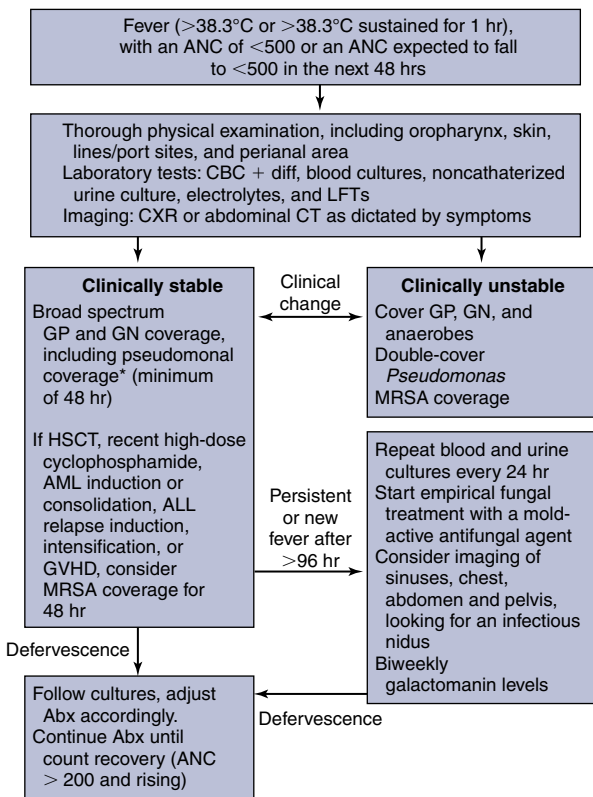
- a. Recipient is transfused with donor stem cells after a myeloablative preparative regimen that includes chemotherapy and often also radiation. Donors are screened for human leukocyte antigen (HLA) subtype matching to recipient. Possible donors include HLA-matched sibling, matched unrelated donors, umbilical cord stem cells, and haploidentical (half-matched) related donors.
- b. Increased level of mismatch between donor and recipient increases graft-versus-tumor effect, but also increases risk for graft-versus-host complications and graft rejection.
- c. Used commonly for AML, ALL (high risk/relapse), myelodysplastic syndrome, juvenile myelomonocytic leukemia (JMML), hemophagocytic lymphohistiocytosis, and a number of nonmalignant hematologic, immunologic, and metabolic disorders.

#### 2. Autologous:

- a. Donor is recipient. After several cycles of conventional chemotherapy, stem cells from patient are harvested (often with assistance of growth factors such as granulocyte colony-stimulating factor [G-CSF] to mobilize), stored, and given back (rescue) after the patient has received what are myeloablative doses of chemotherapy and radiation.
- b. Avoids the complication of graft-versus-host disease (GVHD).
- c. Used for high-risk neuroblastoma, lymphoma, and various high-risk solid tumors.

### C. Engraftment

1. Recipient's bone marrow is repopulated with donor stem cells that proliferate and mature.
2. Usually starts within 2–4 weeks of transplant and presents with an inflammatory response but can be significantly delayed with certain conditions, medications, or infection.



\*Antibiotic selection should account for local resistance patterns as well as prior infections with resistant organisms. Commonly used monotherapies include antipseudomonal  $\beta$ -lactams and fourth-generation cephalosporins or carbapenems.

**FIGURE 22-1**

Guideline for management of fever and neutropenia in children with cancer and/or undergoing hematopoietic stem cell transplantation. Abx, Antibiotics; ALL, acute lymphocytic leukemia; AML, acute myeloid leukemia; ANC, absolute neutrophil count; CBC, complete blood count; CT, computed tomography; CXR, chest x-ray; diff, differential; GN, gram-negative; GP, gram-positive; GVHD, graft-versus-host disease; HSCT, hematopoietic stem cell transplantation; LFTs, liver function tests; MRSA, methicillin-resistant *Staphylococcus aureus*. (Data from Lehrnbecher T, Phillips R, Alexander S, et al. Guideline for the management of fever and neutropenia in children with cancer and/or undergoing hematopoietic stem-cell transplantation. *J Clin Oncol*. 2012;30:4427-4438; Freifeld AG, Bow EJ, Sepkowitz KA, et al. Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2011;52:e56-e93.)

## VII. COMMON COMPLICATIONS OF BONE MARROW TRANSPLANTATION

### A. Acute Graft-Versus-Host Disease (aGVHD)

1. **Etiology:** Donor T-cell-mediated reaction to "foreign" (recipient) antigens. Risk factors include HLA disparity, source of stem cells (peripheral blood > bone marrow > umbilical cord blood).
2. **Presentation:** Classically occurs within 100 days of transplantation, most commonly within 6 weeks, but may occur or persist beyond this time point
  - a. Maculopapular skin rash: Can progress to bullous lesions and toxic epidermal necrolysis
  - b. Laboratory findings: Abnormal liver enzymes (direct hyperbilirubinemia and elevated alkaline phosphatase)
  - c. Upper GI symptoms: Anorexia, dyspepsia, nausea, vomiting
  - d. Lower GI symptoms: Abdominal cramping, diarrhea
3. **Diagnosis:** Triad of rash, abdominal cramping with diarrhea, hyperbilirubinemia. Tissue biopsy of skin or mucosa can provide histologic confirmation. Clinical staging is performed by organ system and dictates the clinical grading of aGVHD ([Table EC 22-A](#)).
4. **Prevention and management:**
  - a. Prophylaxis: Immunosuppression with cyclosporine or tacrolimus; adjuvants are methotrexate and prednisone
  - b. First-line treatment: Steroids commonly used
  - c. Second-line agents: Cyclosporine, tacrolimus, sirolimus, antithymocyte globulin, mycophenolate mofetil, psoralens plus ultraviolet A photopheresis (PUVA) and pentostatin

### B. Chronic Graft-Versus-Host Disease (cGVHD)

1. **Etiology:** Chronic activation of donor immune cells against host antigens. Primary risk factor is prior/current aGVHD. Other risk factors are the same as for aGVHD.
2. **Presentation:** Traditionally presents >100 days after transplant, but may occur earlier either alone or in conjunction with aGVHD:
  - a. Skin is most commonly affected organ, with lichenoid changes on the face, palms, and soles and scleroderma-like changes, predominantly on extremities.
  - b. Cholestasis and hepatitis can be seen with elevated alkaline phosphatase, bilirubin, aspartate aminotransferase, and alanine aminotransferase (AST/ALT).
  - c. GI involvement results in lichenoid changes of oral mucosa, with painful ulcerations that may result in dysphagia. Esophageal strictures, chronic diarrhea, and malabsorption may also be seen.
  - d. Dyspnea and cough may indicate lung involvement, with inflammation and fibrosis that can culminate in bronchiolitis obliterans.
  - e. Xerophthalmia with chronically dry eyes, keratoconjunctivitis, and uveitis.

TABLE EC 22-A

## CLINICAL GRADING OF ACUTE GRAFT-VERSUS-HOST DISEASE

Stage	Skin (% BSA Involved)	Liver (Bilirubin, mg/dL)	Gastrointestinal (GI) System (Diarrhea, mL/day)
1	<25%	2.1–3	501–1000
2	25%–50%	3.1–6	1001–1500
3	50%–general erythroderma	6.1–15	>1500
4	Bullae and/or desquamation	>15	Pain and/or ileus
<b>CLINICAL GRADE</b>			
I	Skin only (stage 1–2)		
II	Stage 1–3 skin OR stage 1 liver OR stage 1 GI		
III	Stage 1–3 skin OR stage 2–3 liver OR stage 2–4 GI		
IV	Stage 4 skin OR stage 4 liver		

3. **Diagnosis:** Clinically diagnosed by classic findings in skin and GI system, as well as evidence of cholestasis. Skin and/or oral mucosa biopsies may be obtained for confirmation. Liver biopsy may be necessary in patients with suspected hepatic cGVHD.

4. **Prevention and management:**

- Treatment should be targeted to affected tissues if cGVHD is limited to a single organ system.
- Steroids continue to be first-line treatment.
- Second-line agents are similar to those used in aGVHD.
- Patients with cGVHD are functionally asplenic and immunosuppressed. They should receive four doses of pneumococcal conjugate vaccine 13 (PCV13) after transplant.

**C. Veno-occlusive Disease (Sinusoidal Obstruction Syndrome)**

1. **Etiology:** Occlusive fibrosis of terminal intrahepatic venules and sinusoids; occurs as a consequence of hematopoietic cell transplantation, hepatotoxic chemotherapy, and/or high-dose liver radiation. Typically occurs within 3 weeks of the insult, most common at the end of the first week after transplant.

2. **Presentation:** Tender hepatomegaly, jaundice, edema, ascites, and sudden weight gain.

3. **Diagnosis:**

- Liver ultrasound with Doppler or MRI showing reversal of portal venous flow
- Elevated bilirubin and ALT/AST
- Prolongation of prothrombin time, decreased factor VII levels (in more severe disease)
- Portal-hepatic venous gradient of  $>10$  mmHg (invasive but sensitive)

4. **Prevention and management:**

- Fluid and sodium restriction.
- Defibrotide has been shown to be successful in 35%–60% of patients with veno-occlusive disease (VOD).

**D. Thrombotic Microangiopathy: Thrombotic Thrombocytopenic Purpura (TTP) or Hemolytic Uremic Syndrome (HUS)**

1. **Etiology:** Post-HSCT, associated with immunosuppressants (cyclosporine, tacrolimus).

2. **Presentation:** Both TTP and HUS present with microangiopathic hemolytic anemia and thrombocytopenia. HUS completes the triad with renal insufficiency/failure, whereas TTP can be associated with neurologic symptoms.

3. **Diagnosis:** Anemia and thrombocytopenia on CBC, schistocytes on peripheral blood smear, hematuria, proteinuria, casts on urinalysis, elevated LDH, decreased haptoglobin, impaired renal function, elevated D-dimer on coagulation panel.

4. **Prevention and treatment:** Urgent plasma exchange if TTP is suspected; blood products, fluid management, dialysis.

### E. Hemorrhagic Cystitis

1. **Etiology:** Pretransplant conditioning regimens (specifically those that include cyclophosphamide, pelvic, or total body irradiation) or viral (adenovirus, BK virus).
2. **Presentation:** Hematuria, dysuria, difficulty voiding.
3. **Diagnosis:** Urine viral polymerase chain reaction (PCR) assay, bacterial cultures, bladder ultrasound, CBC, coagulation studies.
4. **Prevention and management:** Hydration and mesna with preparative regimen. Treatment with aggressive hydration, blood products as indicated, cystoscopy, bladder irrigation, clot evacuation.

### F. Mucositis

1. **Etiology:** Damage to endothelial cells of the GI tract from conditioning regimen, leading to breakdown of the mucosa. Typically peaks in the first 1–2 weeks after transplant.
2. **Presentation:** Oropharyngeal pain, abdominal pain, nausea, vomiting, diarrhea, intolerance of PO intake.
3. **Diagnosis:** Diagnosis is clinical.
4. **Prevention and management:** Supportive care aimed at pain control and nutrition. Local pain control with lidocaine-containing mouthwashes and bicarbonate rinses. Systemic pain control usually requires patient-controlled analgesia (PCA) infusion. Total parenteral nutrition (TPN) is commonly required.

## VIII. HEMATOLOGIC CARE AND COMPLICATIONS

**NOTE:** Transfuse only irradiated and leukoreduced packed red blood cells (PRBCs) and single-donor platelets, cytomegalovirus (CMV)-negative or leukofiltered PRBCs/platelets for CMV-negative patients. Use leukofiltered PRBCs/platelets for those who may undergo bone marrow transplantation (BMT) in the future, to prevent alloimmunization, or for those who have had nonhemolytic febrile transfusion reactions. Many oncology patients have nonhemolytic reactions (temperature elevation, rash, hypotension, respiratory distress) to PRBCs and/or platelet transfusion and will subsequently be premedicated with diphenhydramine and/or acetaminophen for future transfusions.

### A. Anemia

1. **Etiology:** Blood loss, chemotherapy, marrow infiltration, hemolysis
2. **Management:**
  - a. See Chapter 14 for specific details on PRBC transfusions.
  - b. Hematocrit thresholds for PRBC transfusions in cancer patients are based on clinical status and symptoms and are not uncommonly <30 g/dL.

### B. Thrombocytopenia

1. **Etiology:** Chemotherapy, marrow infiltration, consumptive coagulopathy, medications



**2. Management:**

- a. See Chapter 14 for specific details on platelet transfusions.
- b. In general maintain platelet count above 10,000  $\mu\text{L}$  unless patient is actively bleeding or febrile, or before selected procedures (e.g., intramuscular [IM] injection). Consider maintaining platelet counts at higher levels for patients who have brain tumors, recent brain surgery, or history of stroke.

**C. Neutropenia**

1. **Etiology:** Chemotherapy, marrow infiltration, radiation

**2. Management:**

- a. Broad-spectrum antibiotics with concomitant fever (see Fig. 22-1).
- b. GCSF to assist in recovery of neutrophils.
- c. Granulocyte transfusion can be performed in settings of infection or declining clinical status.

**IX. NAUSEA TREATMENT IN CANCER PATIENTS****A. Etiology**

Usual cause is chemotherapy treatment. Also suspect opiate therapy, GI and CNS radiotherapy, obstructive abdominal process, elevated ICP, certain antibiotics, or hypercalcemia.

**B. Presentation**

1. **Acute:** Emesis within 24 hours of starting chemotherapy; occurs in one third of patients despite treatment.
2. **Delayed:** Emesis occurring >24 hours after chemotherapy. Risk factors include female gender, prior acute emesis, highly emetogenic agents (e.g., cisplatin).
3. **Anticipatory:** Emesis before chemotherapy administration.

**C. Therapy**

Hydration plus one or more antiemetic medications (see Formulary for dosing)

1. **Serotonin (5-HT<sub>3</sub>) antagonists:** Ondansetron, dolasetron, granisetron, or palonosetron. Usually a first-line therapy. Best for acute emesis. Risk of QT prolongation, widening of QRS.
2. **Histamine-1 antagonist:** Diphenhydramine; also cyproheptadine (with anticholinergic side effect of appetite stimulation).
3. **Steroids:** Dexamethasone; especially helpful in patients with brain tumor and as prophylaxis for delayed symptoms; synergy with 5-HT<sub>3</sub> antagonists.
4. **Benzodiazepines:** Lorazepam; used as an adjunct antiemetic agent.
5. **Metoclopramide:** Use diphenhydramine to reduce risk of extrapyramidal symptoms (EPS).
6. **Phenothiazines:** Promethazine, chlorpromazine; use diphenhydramine to reduce risk of EPS.
7. **Cannabinoids:** Dronabinol; can be helpful in resistant cases, especially in patients with large tumor burden. May also be used as an appetite stimulant in malnourished patients.
8. **Substance P and neurokinin-1 receptor antagonist:** Aprepitant; avoid with certain chemotherapy drugs (e.g., ifosfamide, etoposide).

## X. ANTIMICROBIAL PROPHYLAXIS IN ONCOLOGY PATIENTS (TABLE 22-3)

**NOTE:** Treatment length and dosage may vary per protocol.

**TABLE 22-3**

### ANTIMICROBIAL PROPHYLAXIS IN ONCOLOGY PATIENTS

Organism	Medication	Indication
<i>Pneumocystis jiroveci</i>	TMP-SMX, atovaquone, dapsone, or pentamidine	Chemotherapy and BMT per protocol (usually at least 6 mo after chemotherapy, 12 mo after BMT)
HSV	Acyclovir (dosing is different for zoster, varicella, and mucocutaneous HSV)	After BMT if patient or donor is HSV or CMV positive; recurrent zoster
<i>Candida albicans</i>	Fluconazole or voriconazole	After BMT (usually at least 28 days)
Gram-positive organisms	Penicillin	After BMT (usually at least 1 mo)

BMT, Bone marrow transplantation; CMV, cytomegalovirus; HSV, herpes simplex virus; TMP-SMX, trimethoprim-sulfamethoxazole.

## XI. BEYOND CHILDHOOD CANCER: TREATING A CANCER SURVIVOR<sup>1,2,6</sup>

### A. Understand the Treatment Regimen

- Identify all components of therapy received:** Comprehensive treatment summary from oncologist, summarizing:
  - Diagnosis: Site/stage, date, relapse
  - Chemotherapy: Cumulative doses, high dose vs. low dose for methotrexate and cytarabine
  - Radiation: Locations, cumulative dose
  - Surgeries: Dates, sites, resection
  - BMT: Preparation regimen, source of donor cells (including degree of HLA mismatch), GVHD, complications
  - Investigational treatments
  - Adverse drug reactions or allergies
- Follow up with any investigational treatments used.**
- Determine any potential problems by organ system,** and devise plan for routine evaluation.

### B. Common Late Effects<sup>1,2,7,NaN</sup> (See Table EC 22-B)

Also see <http://www.survivorshipguidelines.org/>.

TABLE EC 22-B

LATE EFFECTS OF CANCER TREATMENT BY ORGAN SYSTEM/SITE<sup>1,2,7,NAN</sup>

Organ System/ Site	Treatment Modality	Associated Late Effects	Suggested Monitoring
CNS/endocrine	Radiation therapy Chemotherapy: intrathecal high-dose methotrexate	Precocious puberty, growth hormone deficiency, cogni- tive dysfunction, ototoxicity, peripheral neuropathy	Neuroendocrine monitoring, neuropsychological testing
Vision	Radiation therapy	Cataracts, optic neuropathy	Routine ophthalmology follow-up
Hearing	Radiation therapy Chemotherapy: platinum agents	Ototoxicity, sensorineural hearing loss	Regular audiology follow- up and evaluation
Thyroid	Radiation therapy	Malignancy, hyperthyroid, hypothyroid	Thyroid function testing
Cardiac	Radiation therapy Chemotherapy: anthracyclines	Cardiomyopathy, peri- carditis, coronary artery disease, arrhythmias, cardiomyopathies	ECG, echocardiogram
Pulmonary	Radiation therapy Chemotherapy: bleomycin	Pulmonary fibrosis, restrictive lung disease	Pulmonary function tests with DLCO
Hepatic	Radiation therapy Chemotherapy: 6-TG, methotrexate, 6-MP, dactinomycin, busulfan	Hepatic fibrosis, portal hypertension, VOD	LFTs, liver ultrasound with Doppler
Renal	Radiation therapy Chemotherapy: platinum agents, high-dose meth- otrexate, ifosfamide	Renal insufficiency/failure	UA, blood pressure, electrolytes, creatinine clearance, GFR
Urologic	Radiation therapy Chemotherapy: cyclophos- phamide, ifosfamide	Cancer, fibrosis, hemorrhagic cystitis	Cystoscopy, bladder ultrasound, UA, urine culture
Gonadal/repro- ductive	Radiation therapy Chemotherapy: alkylating agents	Delayed puberty, ovarian failure, infertility, testosterone deficiency	LH, FSH, estradiol, gynecologic evaluation Semen analysis, testosterone
Musculoskel- etal	Radiation therapy Chemotherapy: metho- trexate, corticosteroids	Osteoporosis/osteopenia, osteonecrosis	DEXA scan; calcium and vitamin D supplementation may be recommended for high-risk patients
Secondary malignan- cies	Radiation therapy Chemotherapy: alkylating agents, topoisomerase II inhibitors, platinum agents, cyclophos- phamide	For radiation, location is site-dependent; associ- ated secondary malignan- cies include CNS, breast, thyroid, melanoma, solid tumors and sarcomas Leukemia (alkylating agents) Bladder cancer (cyclophosphamide)	Yearly comprehensive history and physical, routine blood work, recommended follow-up for specific treatment modalities

CNS, Central nervous system; DEXA, dual-energy x-ray absorptiometry; DLCO, diffusing capacity of lung for carbon monoxide; ECG, electrocardiogram; FSH, follicle-stimulating hormone; GFR, glomerular filtration rate; LFT, liver function test; LH, luteinizing hormone; UA, urinalysis; VOD, vaso-occlusive disease.

**1. Vaccinations in oncology patients:**

- a. After treatment is finished, time to full recovery of adaptive immune function is variable. Typically 3–6 months for patients treated with chemotherapy but no HSCT; for patients treated with HSCT, a minimum of several months and often >1 year.
  - b. Chronic GVHD: Functionally asplenic and immunosuppressed. Patients are at high risk for pneumococcal disease.
  - c. Inactivated influenza vaccination should be considered for all oncology patients. Family members should be encouraged to get vaccinated as well.
  - d. **Patients treated with chemotherapy but no HSCT:**
    - (1) Administer all recommended vaccines before starting therapy.
    - (2) Consider vaccination with DTaP (diphtheria and tetanus toxoids and acellular pertussis), IPV (inactivated poliovirus vaccine), Hib (*Haemophilus influenzae* type b), and MMR (measles, mumps, rubella) starting 3–6 months after completing chemotherapy. Consider VZV (varicella-zoster virus) vaccine 12 months after chemotherapy.
  - e. **Patients treated with HSCT:**
    - (1) Consider these patients unimmunized and needing a full catch-up immunization schedule. Schedule may have to be altered if chronic GVHD or immunosuppression is present.
    - (2) At 6–12 months after HSCT, can begin series of three doses of DTaP (<7 years of age) or Tdap (tetanus and diphtheria toxoids and acellular pertussis) (>7 years of age), three doses of Hib vaccine, three doses of hepatitis B vaccine, three doses of IPV, and one dose of meningococcal vaccine.
    - (3) Three doses of PCV13 should be given starting 3 months after HSCT. Patients >2 years of age with no cGVHD should receive one dose of 23-valent pneumococcal polysaccharide vaccine 12 months after HSCT. Patients with cGVHD should receive fourth dose of PCV13.
    - (4) At 24 months after HSCT, patients can receive one dose (adolescents) or two doses (children) of MMR. VZV vaccination can be considered in seronegative patients without cGVHD.
2. **Organ system-specific late effects** (see [Table EC 22-B for more specific information](#))

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# Chapter 23

## Palliative Care

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### I. PALLIATIVE CARE

#### A. Website

For additional information please refer to American Academy of Hospice and Palliative Medicine at [www.aahpm.org](http://www.aahpm.org)

#### B. Definition<sup>1,2</sup>

Palliative care is the active total care of the child's body, mind, and spirit with the intent to prevent and relieve suffering. It supports the best quality of life for the child and family beginning at diagnosis of a life-limiting condition and continuing regardless of whether the child receives treatment. Hospice care is a form of palliative care that focuses on the end of life and bereavement. Effective palliative care requires an interdisciplinary approach that works with child and family to determine goals of care. This is best accomplished when the palliative care team is involved as early in the child's course of illness as possible (Fig. 23-1).

#### C. Palliative Care Team Composition

1. **Child and family**
2. **Physician:** Primary care physician, specialist attending physician, fellow, resident, intern
3. **Nurses:** Primary nurse, charge nurse, home care nurse, hospice nurse
4. **Pain specialist and hospice palliative care specialist**
5. **Social worker**
6. **Child life specialist**

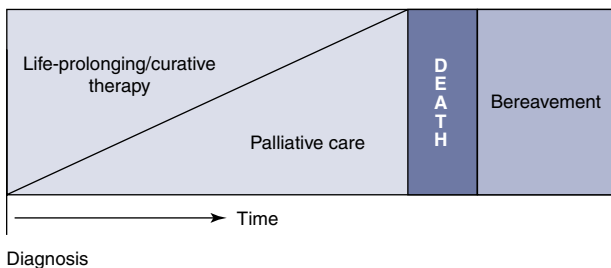


FIGURE 23-1

Current accepted model for palliative care.

7. **Pastoral care**
8. **Patient care coordinator and case manager**
9. **Bereavement coordinator**
10. **Community resources:** School, faith community, hospice program

## II. COMMUNICATION AND DECISION MAKING

### A. Decision-Making Tools (DMT)<sup>3</sup>

1. **Provides consistent, reliable format for discussion and formulation of plan of care.** Patients, families, and health care providers all participate in the process.
2. **Four domains of DMT should be updated regularly,** especially during “non-crisis” periods.
  - a. Medical indications: Diagnosis, symptoms, risk/benefits of treatment, cure/relapse rate, complications
  - b. Patient and family preferences: Information, decision making, desire for autonomy and privacy
  - c. Quality of life: Important activities of child, important relationships, emotional/spiritual well-being
  - d. Contextual issues: Identifying family unit, home environment, financial barriers, legal issues, cultural and spiritual beliefs

### B. Family Meetings<sup>4</sup>

1. **Prepare the people and the messages.**
  - a. Why are you having the meeting?
  - b. Do you have all the information you need?
  - c. Are all clinicians in agreement about the patient's condition and the recommendations?
  - d. Are there decisions to be made?
  - e. Who should attend? Patient, parents, other important individuals? Which clinicians?
  - f. Who will take the lead role as the facilitator?
2. **Choose a private location with minimal distraction.**
3. **Begin by introducing all participants and the purpose of the meeting.**
  - a. Check whether any additional issues for discussion have arisen.
4. **Assess what the family knows and expects.**
  - a. What is their current understanding of the patient's condition?
  - b. What have they already been told?
5. **Describe the clinical situation.**
  - a. A brief, clear overview first. What is the big picture?
  - b. Then ask if the family wants and is ready for more details.
  - c. Periodically ask whether what you are saying is clear and makes sense.
6. **Encourage each member of the family to express concerns and questions.** Ask until there are no more questions.
7. **Explore the patient's and family's values and how they should influence decision making.**
  - a. Has there been any prior experience with serious medical decisions for this patient or another family member?

- b. How does the family decide what is best?
- c. Are there guides or principles that help the family decide?
- 8. Propose goals for the patient's care that reflect the stated values.**
  - a. Begin with what treatments or interventions you recommend as beneficial and that support the goals of care.
  - b. If there are treatments you would not recommend because they do not support the overall goals of care, mention them later with your reason for not recommending.
  - c. Be prepared to listen compassionately and negotiate.
- 9. Provide a concrete follow-up plan.**
  - a. Summarize the plan for care.
  - b. Agree on when to talk or meet again.

**C. Child Participation**

- 1. Development of death concepts in children<sup>5-8</sup> (Table 23-1).**
- 2. Child's capacity to participate in health care decisions.** Minor children can participate meaningfully in decision making if they demonstrate all of the following:
  - a. Communicate understanding of the medical information
  - b. State his or her preference
  - c. Communicate understanding of the consequences of decisions

**D. Advance Directive**

- 1. Adolescents 18 years of age and older** can name another adult to make health care decisions if they are unable to speak for themselves.
- 2. Health care team can help patients voice preferences** for future health care decisions.

**TABLE 23-1**

**CONCEPTUALIZATION OF DEATH IN CHILDREN**

Age Range	Characteristics	Concepts of Death	Interventions
0–2 yr	Achieve object permanence May sense something is wrong	None	Provide maximal comfort with familiar persons and favorite toys.
2–6 yr	Magical thoughts	Believes death is temporary Does not personalize death Believes death can be caused by thoughts	Minimize separation from parents; correct perceptions that the illness is punishment.
6–12 yr	Concrete thoughts	Understands death can be personal Interested in details of death	Be truthful, evaluate fears, provide concrete details if requested, allow participation in decision making.
12–18 yr	Reality becomes objective Capable of self-reflection	Searches for meaning, hope, purpose, and value of life	Be truthful, allow expression of strong feelings, allow participation in decision making.



### III. LEGACY AND MEMORY MAKING

#### A. Memory Making

1. **Provide opportunities for the family to participate in memory making** (e.g., create memory boxes/packets, lock of hair, foot/hand molds or prints, videos, photographs).
2. **Older children may have specific wishes for funeral, memorial, or distribution of personal belongings.**

#### B. Rituals

Allow for culturally important rituals to be performed by the family (e.g., baptism, bathing, music, faith ceremonies or prayer).

#### C. Being at Home

For many children and families, the opportunity to be at home together, especially as a child approaches the end of life, is a top priority. Be sure to ask families about this early, before it is too late to transfer the patient and assess what preparations have to be made.

### IV. DECISIONS TO LIMIT INTERVENTIONS

#### A. Do Not Attempt Resuscitation (DNAR)

1. **In the event of cardiorespiratory arrest**, cardiopulmonary resuscitation (CPR) is automatically initiated in hospitals by health care teams and in community settings by first responders. For patients with life-threatening conditions, CPR may not prolong or enhance quality of life, making it inconsistent with goals of care. The health care team should offer patients and families the option of forgoing CPR and other resuscitative interventions as part of an overall care plan that emphasizes comfort and quality of living (Box 23-1).
2. **If this option is desired**, physician must write a specific order *not* to attempt CPR (e.g., “In the event of cardiopulmonary arrest, do not attempt

#### BOX 23-1

##### SAMPLE FROM STATE OF MARYLAND EMS/DNAR FORMS AND BRACELET AUTHORIZATION FORM

The physician must sign the *Physician Certification and Order* and initial ONLY ONE of the two options on the form.

##### Option A:

Maximum Efforts to Prevent Cardiac/Respiratory Arrest  
DNAR if Arrest Occurs—No CPR

##### Option B:

Supportive Care Prior to Cardiac/Respiratory Arrest  
DNAR if Arrest Occurs—No CPR

**NOTE:** If a valid EMS/DNAR Order is located after resuscitation has begun, EMS personnel may withdraw resuscitation.

**NOTE:** Ambulance personnel cannot honor specific instructions in advance directives that do not conform to the care selections in the *Physician Certification and Order* (e.g., wants intubation but no CPR).

resuscitation.”). Orders must follow local emergency medical services (EMS) policies for patients at home.

### B. Do Not Escalate Treatment

When escalation of treatment no longer supports the goals of care, offer patients and families the option to forgo treatment changes even as the patient's condition worsens. Because death is expected, DNAR must also be discussed. Examples of such requests include:

1. **Do not increase the dose of current medications** (e.g., vasopressors).
2. **Do not add new medications** (e.g., antibiotics).
3. **Do not initiate new interventions** (e.g., dialysis, mechanical ventilation).
4. **Initiate and increase interventions** to treat pain and reduce suffering.

### C. Discontinuing Current Interventions

When death is expected regardless of intervention, especially if current interventions are prolonging the dying process, patients and families can be offered the option of discontinuing these interventions (e.g., “Discontinue blood products, monitors, mechanical ventilation, medically provided hydration or nutrition.”). Because death is expected, DNAR must also be discussed.

### D. State Forms

MOLST (Medical Orders for Life-Sustaining Treatment) and POLST (Physician Orders for Life-Sustaining Treatment) Forms

1. **These are portable and enduring medical order forms** completed by patients or their authorized decision makers and signed by a physician. They contain orders regarding CPR and other life-sustaining treatments.
2. **If a state offers one of these forms**, the orders are valid for EMS providers as well as all health care providers and facilities within that state.
3. **A copy must be provided to the patient or authorized decision maker** within 48 hours of completion, or sooner if the patient is to be transferred.
4. **Please refer to your state's laws prior to completion of any documentation.** Additional information can be found at [www.polst.org](http://www.polst.org).

## V. BODY, MIND, AND SPIRIT CHANGES AS DEATH APPROACHES

### A. Physical Changes

1. **Cardiac:** Blood pressure decreases, heart rate increases, and pulse becomes weaker.
2. **Circulation:** Cool extremities; cyanosis of fingers, nails, lips; mottling of skin
3. **Gastrointestinal:** Metabolism slows and appetite gradually decreases. Liquids are preferred to solids. The body will become naturally dehydrated, and fevers may occur as death approaches. Provide relief with ice chips, moist mouth swabs, antipyretic per rectum.

4. **Respiratory:** Variable pattern of breathing (tachypnea followed by periods of apnea); congestion secondary to secretion build-up; provide relief as follows:
  - a. Turn patient every few hours, elevate head of bed, provide frequent mouth care, hyoscyamine as needed.
  - b. Relief of air hunger: Morphine and lorazepam as needed, oxygen for comfort.
  - c. **NOTE:** Deep suctioning is not helpful.
5. **Sensation changes:** Senses become overactive. Bright lights, noise, or television may be upsetting. Hearing is typically the last sense to diminish. Provide relief by dimming lights, reducing noise, and providing soft background music.
6. **Sleep:** Need for sleep increases as death approaches. Occasionally the child exhibits a surge of energy to play, eat, or socialize.

### B. Emotional Changes

Detachment from the outside world: Reduced need to socialize leads to pulling inward of thoughts, emotions, and fears. Listen and reassure family about decreased interactions.

### C. Mental Changes

Mental status: Confusion, restlessness, agitation, delirium. Provide relief by keeping child oriented to surroundings, surrounding him/her with family as a way to reinforce safety, and speaking in calm tones. Use lorazepam and haloperidol as needed.

### D. Spiritual Changes

Spiritual: Child may call out or reach out for loved ones who are not physically present. Reassure the family that this is not unusual during the dying process.

## VI. LAST HOURS: MEDICATION AND MANAGEMENT <sup>10</sup> (TABLE 23-2)

## VII. DEATH PRONOUNCEMENT <sup>11</sup>

Residents may be called to pronounce the death of a patient in the hospital. This important task should be carried out with competence, compassion, and respect.

### A. Preparation

1. **Know the child's name and gender.**
2. **Be prepared to answer simple pertinent questions** from family and friends.
3. **Consult with nursing staff for relevant information:** recent events, family response, family dynamics.
4. **Determine the need and call for interdisciplinary support:** social work, child life, pastoral care, bereavement coordinator.

### B. Entering the Room

1. **Enter quietly and respectfully** along with the primary nurse.

TABLE 23-2

## COMMON MEDICATIONS USED FOR SYMPTOMATIC RELIEF IN PALLIATIVE CARE

Indication	Medication	Initial Regimen
Pain	Morphine	0.3 mg/kg/dose PO, SL, PR Q2–4 hr* 0.1–0.2 mg/kg/dose IV Q2–4 hr* <b>NOTE:</b> Morphine should be titrated to symptomatic relief.
Dyspnea	Morphine	0.1–0.25 mg/kg/dose PO, SL, PR Q2–4 hr 0.05–0.1 mg/kg/dose IV Q2–4 hr 2.5–5 mg/3 mL normal saline nebulizer Q4hr <b>NOTE:</b> Nebulized morphine can cause severe bronchospasm and worsen dyspnea. Nebulized fentanyl may be preferred.
Agitation	Lorazepam	0.05 mg/kg/dose PO, IV, SL, PR Q4–8 hr
	Haloperidol	0.01–0.02 mg/kg/dose PO, SL, PR Q8–12 hr
Pruritus	Diphenhydramine	0.5–1 mg/kg/dose PO, IV Q6–8 hr
Nausea and vomiting	Prochlorperazine	0.1–0.15 mg/kg/dose PO, PR Q6–8 hr
	Ondansetron	0.15 mg/kg/dose PO, IV Q6–8 hr
Seizures	Diazepam	0.3–0.5 mg/kg/dose PR Q2–4 hr
	Lorazepam	0.05–0.1 mg/kg/dose IV Q2–4 hr
Secretions	Hyoscyamine	0.03–0.06 mg/dose PO, SL Q4hr (if <2 yr) 0.06–0.12 mg/dose PO, SL Q4hr (if 2–12 yr) 0.12–0.25 mg/dose PO, SL Q4hr (if >12 yr)

\*Infants <6 mo should receive one third to one half the dose.

IV, Intravenous; PO, oral; PR, rectal; SL, sublingual.

Adapted from Himelstein BP, Hilden JM, Boldt AM, et al. Pediatric palliative care. *N Engl J Med*. 2004;350:1752–1762.

## 2. Introduce yourself and identify your role:

- “I am Dr. \_\_\_\_\_, the doctor on call.”
- Determine the relationships of those in the room.
- Inform the family of the purpose of your visit (“I am here to examine your child”), and invite them to remain in the room.

## C. Procedure for Pronouncement

- Check ID bracelet and pulse.
- Respectfully check response to tactile stimuli.
- Check for spontaneous respirations.
- Check for heart sounds.
- Record the time of death.
- Inform the family of death.
- Offer to contact other family members.
- Remember to convey sympathy: “I am so sorry for your loss.”

## D. Document Death in the Chart

- Write date, time of death, and the provider pronouncing the death.
- Document absence of pulse, respirations, and heart sounds.
- Identify family members who were present and informed of death.
- Document notification of attending physician.

### E. Death Certificate

1. **Locate a copy of a sample death certificate for reference.**
2. **Use BLACK INK only and complete *Physician sections*.**
- a. **NOTE:** Do *NOT* use abbreviations (e.g., spell out the month: January 31 and not 1/31).
- b. **NOTE:** Do *NOT* cross out or use white out; must begin again if mistakes are made.
- c. **NOTE:** Cardiopulmonary or respiratory arrest is *NOT* an acceptable primary cause of death.

### F. Autopsy Consent

1. **Obtain family consent if indicated.**
2. **Plan follow-up to contact and review autopsy results.**

## VIII. AFTER DEATH—BEREAVEMENT<sup>11</sup>

### A. Etiquette

Families want to know that their children are not forgotten. Sending condolence cards, attending funerals, and contacting the family weeks to months later are all appropriate physician activities that are deeply valued by bereaved families. Respectful listening to families and sharing memories of the child help provide support during bereavement.

### B. Available Services<sup>12</sup>

Be familiar with available services: pastoral care, social work, bereavement coordinator, community support groups, counseling services, bereavement follow-up programs.

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# Chapter 24

## Pulmonology

Margaret Grala, MD

24

 See additional content on Expert Consult

### I. WEBSITES

American Lung Association: <http://www.lung.org>

Cystic Fibrosis Foundation: <http://www.cff.org>

American Academy of Allergy, Asthma and Immunology:  
<http://www.aaaai.org>

National Heart Lung and Blood Institute: National Asthma Education and  
Prevention Program: <http://www.nhlbi.nih.gov>

American Thoracic Society: <http://www.thoracic.org>

### II. RESPIRATORY PHYSICAL EXAMINATION

#### A. Normal Respiratory Rates in Children (Table 24-1)

#### B. Inspection

Evaluate for chest wall abnormalities (barrel chest, pectus excavatum, or pectus carinatum), symmetry, accessory muscle use, cyanosis of lips, skin, or nails, or digital clubbing.

#### C. Palpation and Percussion

#### D. Auscultation (Table 24-2)

### III. EVALUATION OF PULMONARY GAS EXCHANGE

#### A. Pulse Oximetry<sup>1-5</sup>

1. **Pulse oximetry** ( $\text{SpO}_2$ ) is an indirect measurement of arterial  $\text{O}_2$  saturation ( $\text{Sao}_2$ ) estimated by light absorption characteristics of oxygenated and deoxygenated hemoglobin through the skin in peripheral blood.

TABLE 24-1

NORMAL RESPIRATORY RATES IN CHILDREN

Age (yr)	Respiratory Rate (breaths/min)
0–1*	24–38
1–3	22–30
4–6	20–24
7–9	18–24
10–14	16–22
14–18	14–20

\*Slightly higher respiratory rates (i.e., 40–50 breaths/min) in the neonatal period may be normal in the absence of other signs and symptoms.

Data from Bardella J. Pediatric advanced life support: a review of the AHA recommendations. *Am Fam Phys.* 1999;60:1743–1750.

**TABLE 24-2**

**RESPIRATORY AUSCULTATION**

Sound	Description	Possible Causes
Crackles (rales)	Intermittent scratchy, bubbly noises Heard predominantly on inspiration Produced by reopening of airways closed on previous expiration	Bronchiolitis, pulmonary edema, pneumonia, asthma
Wheezes	Continuous, high-pitched, musical sound predominantly on expiration	Asthma, bronchiolitis, foreign body
Rhonchi	Continuous, low-pitched, nonmusical sound	Pneumonia, cystic fibrosis
Stridor	High-pitched, harsh, blowing sound Heard predominantly on inspiration	Croup, laryngomalacia, subglottic stenosis, allergic reaction, vocal cord dysfunction

**2. Important uses:**

- Rapid and continuous assessment of oxygenation in acutely ill patients or patients requiring oxygen therapy
- Assessment of oxygen requirements during feeding, sleep, exercise, or sedation
- Monitoring of physiologic effects of apnea and bradycardia

**3. Limitations:**

- Measures oxygen saturation, not O<sub>2</sub> delivery to tissues. A marginally low saturation in an anemic patient may be more significant because of their reduced O<sub>2</sub>-carrying capacity.
- Insensitive to hyperoxia because of the sigmoid shape of the oxyhemoglobin curve (Fig. 24-1).
- Artificially increased: Carboxyhemoglobin levels >1%–2% (e.g., in chronic smokers or with smoke inhalation).
- Artificially decreased: Patient motion, intravenous dyes (methylene blue, indocyanine green), opaque nail polish, and methemoglobin levels >1%.
- Unreliable when pulse signal is poor: Hypothermia, hypovolemia, shock, edema, or movement artifact.
- Spo<sub>2</sub> reading often does not correlate with Pao<sub>2</sub> in sickle cell disease.<sup>6</sup>

**4. Oxyhemoglobin dissociation curve** (see Fig. 24-1)

**B. Capnography**

- Measures CO<sub>2</sub> concentration of expired gas** by infrared spectroscopy or mass spectroscopy.
- End-tidal CO<sub>2</sub> (ETCO<sub>2</sub>) correlates with Paco<sub>2</sub>** (usually within 5 mm Hg in healthy subjects).
- Can be used for demonstrating proper placement of an endotracheal tube**, continuous monitoring of CO<sub>2</sub> trends in ventilated patients, and monitoring ventilation during polysomnography.

**C. Blood Gases**

- Arterial blood gas (ABG):** Most accurate way to assess oxygenation (Pao<sub>2</sub>), ventilation (Paco<sub>2</sub>), and acid-base status (pH and HCO<sub>3</sub><sup>-</sup>). See Chapter 27 for normal mean values.



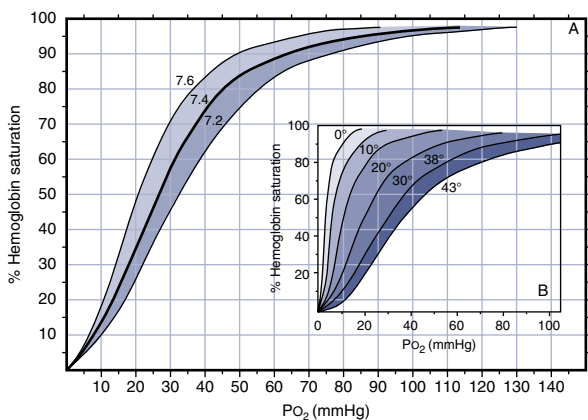


FIGURE 24-1

Oxyhemoglobin dissociation curve. **A**, Curve shifts to the left as pH increases. **B**, Curve shifts to the left as temperature decreases. (Data from Lanbertsten CJ. *Transport of oxygen, CO<sub>2</sub>, and inert gases by the blood*. In: Mountcastle VB, ed. *Medical Physiology*. 14th ed. St Louis: Mosby, 1980.)

- Venous blood gas (VBG):**  $P_{vCO_2}$  averages 6–8 mmHg higher than  $P_{aCO_2}$ , and venous pH is slightly lower than arterial pH. Measurement is strongly affected by the local circulatory and metabolic environment.
- Capillary blood gas (CBG):** Correlation with ABG generally best for pH, moderate for  $P_{CO_2}$ , and worst for  $P_{O_2}$ .

#### D. Analysis of Acid-Base Disturbances<sup>7-9</sup>

- Determine primary disturbance**, then assess for mixed disorder by calculating expected compensatory response (Fig. 24-2 and Table 24-3).

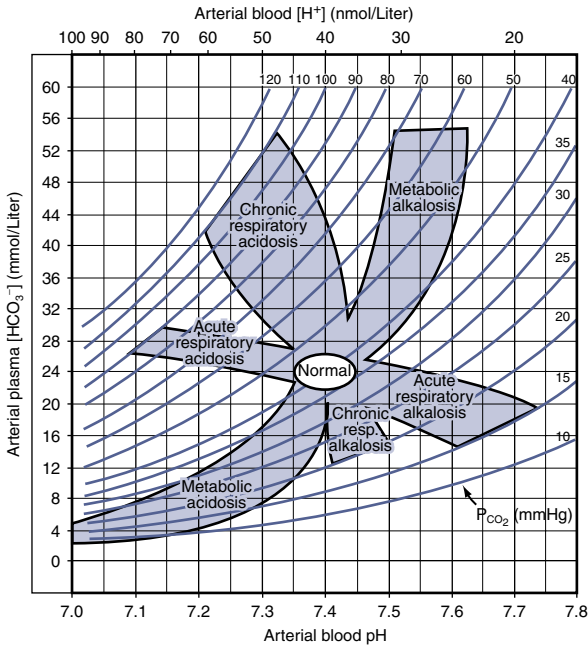
### IV. PULMONARY FUNCTION TESTS

Provide objective and reproducible measurements of airway function and lung volumes. Used to characterize disease, assess severity, and follow response to therapy.

#### A. Peak Expiratory Flow Rate (PEFR)

Maximal flow rate generated during a forced expiratory maneuver.

- Often used to follow the course of asthma and response to therapy** by comparing a patient's PEFR with the previous "personal best" and the normal predicted value
  - Limitations: Normal predicted values vary across different racial groups. Measurement is effort dependent and cannot be done reliably by many young children, and PEFR is insensitive to small airway function.
- Normal predicted PEFR values for children** (Table 24-4)



**FIGURE 24-2**

Interpretation of arterial blood gases. (Modified from Siggaard-Anderson O. *The Acid-Base Status of the Blood*. 4th ed. Copenhagen: Munksgaard, 1976.)

**TABLE 24-3**

**CALCULATION OF EXPECTED COMPENSATORY RESPONSE**

Disturbance	Primary Change	pH*	Expected Compensatory Response
Acute respiratory acidosis	$\uparrow \text{Paco}_2$	$\downarrow \text{pH}$	$\uparrow \text{HCO}_3^-$ by 1 mEq/L for each 10 mmHg rise in $\text{Paco}_2$
Acute respiratory alkalosis	$\downarrow \text{Paco}_2$	$\uparrow \text{pH}$	$\downarrow \text{HCO}_3^-$ by 1–3 mEq/L for each 10 mmHg fall in $\text{Paco}_2$
Chronic respiratory acidosis	$\uparrow \text{Paco}_2$	$\downarrow \text{pH}$	$\uparrow \text{HCO}_3^-$ by 4 mEq/L for each 10 mmHg rise in $\text{Paco}_2$
Chronic respiratory alkalosis	$\downarrow \text{Paco}_2$	$\uparrow \text{pH}$	$\downarrow \text{HCO}_3^-$ by 2–5 mEq/L for each 10 mmHg fall in $\text{Paco}_2$
Metabolic acidosis	$\downarrow \text{HCO}_3^-$	$\downarrow \text{pH}$	$\downarrow \text{Paco}_2$ by 1–1.5 times fall in $\text{HCO}_3^-$
Metabolic alkalosis	$\uparrow \text{HCO}_3^-$	$\uparrow \text{pH}$	$\uparrow \text{Paco}_2$ by 0.25–1 times rise in $\text{HCO}_3^-$

\*Pure respiratory acidosis (or alkalosis): 10-mm Hg rise (fall) in  $\text{Paco}_2$  results in an average 0.08 fall (rise) in pH. Pure metabolic acidosis (or alkalosis): 10-mEq/L fall (rise) in  $\text{HCO}_3^-$  results in an average 0.15 fall (rise) in pH.  
Data from Schrier RW. *Renal and Electrolyte Disorders*. 3rd ed. Boston: Little, Brown, 1986.

TABLE 24-4

## PREDICTED AVERAGE PEAK EXPIRATORY FLOW RATES FOR NORMAL CHILDREN

Height Inches (cm)	PEFR (L/min)	Height Inches (cm)	PEFR (L/min)
43 (109)	147	56 (142)	320
44 (112)	160	57 (145)	334
45 (114)	173	58 (147)	347
46 (117)	187	59 (150)	360
47 (119)	200	60 (152)	373
48 (122)	214	61 (155)	387
49 (124)	227	62 (157)	400
50 (127)	240	63 (160)	413
51 (130)	254	64 (163)	427
52 (132)	267	65 (165)	440
53 (135)	280	66 (168)	454
54 (137)	293	67 (170)	467
55 (140)	307		

PEFR, Peak expiratory flow rate.

Data from Voter KZ. Diagnostic tests of lung function. *Pediatr Rev.* 1996;17:53-63.

## B. Maximal Inspiratory and Expiratory Pressures<sup>10,11</sup>

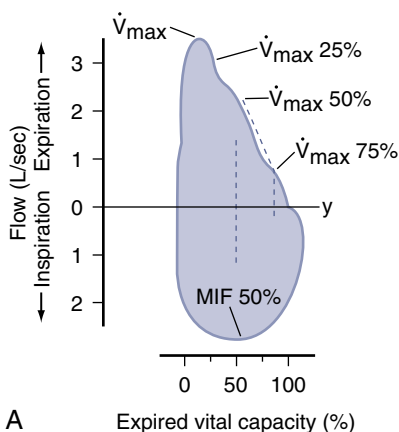
Maximal pressure generated during inhalation and exhalation against a fixed obstruction.

1. **Used as a measure of respiratory muscle strength.**
2. **Maximal inspiratory pressure (MIP)** is in the range of 80–120 cm H<sub>2</sub>O at all ages. Maximum expiratory pressure (MEP) increases with age and is greater in males.
3. **A low MIP may be an indication for ventilatory support, and a low MEP correlates with decreased effectiveness of coughing.**

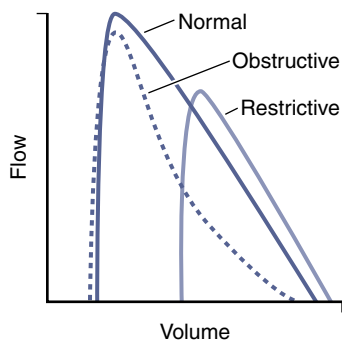
## C. Spirometry (for Children ≥6 Years)

Plot of airflow versus time during rapid, forceful, and complete expiration from total lung capacity (TLC) to residual volume (RV). Useful to characterize different patterns of airway obstruction (Fig. 24-3). Usually performed before and after bronchodilation to assess response to therapy or after bronchial challenge to assess airway hyperreactivity.

1. **Important definitions** (Fig. 24-4)
  - a. **Forced vital capacity (FVC):** Maximum volume of air exhaled from the lungs after a maximum inspiration. Bedside measurement of vital capacity with a handheld spirometer can be useful in confirming or predicting hypoventilation associated with muscle weakness.
  - b. **Forced expiratory volume in 1 second (FEV<sub>1</sub>):** Volume exhaled during the first second of the FVC maneuver.
  - c. **Forced expiratory flow (FEF<sub>25-75</sub>):** Mean rate of airflow over the middle half of the FVC between 25% and 75% of FVC. Sensitive to medium and small airway obstruction.
2. **Interpretation of spirometry and lung volume readings** (Table 24-5).



A



B

FIGURE 24-3

**A**, Normal flow-volume curve. **B**, Worsening intrathoracic airway obstruction as in asthma or cystic fibrosis. (**B**, Data from Baum GL, Wolinsky E. Textbook of Pulmonary Diseases. 5th ed. Boston: Little, Brown, 1994.)

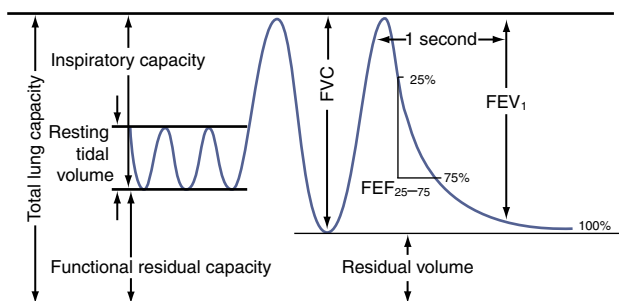


FIGURE 24-4

Lung volumes.  $FEV_{25-75}$ , Forced expiratory flow between 25% and 75% of FVC;  $FEV_1$ , forced expiratory volume in 1 second; FVC, forced vital capacity.

TABLE 24-5

## INTERPRETATION OF SPIROMETRY AND LUNG VOLUME READINGS

	Obstructive Disease (Asthma, Cystic Fibrosis)	Restrictive Disease (Interstitial Fibrosis, Scoliosis, Neuromuscular Disease)
<b>SPIROMETRY</b>		
FVC*	Normal or reduced	Reduced
$FEV_1^*$	Reduced	Reduced <sup>§</sup>
$FEV_1/FVC^\dagger$	Reduced	Normal
$FEF_{25-75}$	Reduced	Normal or reduced <sup>§</sup>
PEFR*	Normal or reduced	Normal or reduced <sup>§</sup>
<b>LUNG VOLUMES</b>		
TLC*	Normal or increased	Reduced
RV*	Increased	Reduced
RV/TLC <sup>‡</sup>	Increased	Unchanged
FRC	Increased	Reduced

\*Normal range:  $\pm 20\%$  of predicted.

<sup>†</sup>Normal range:  $>85\%$ .

<sup>‡</sup>Normal range:  $20 \pm 10\%$ .

<sup>§</sup>Reduced proportional to FVC.

$FEF_{25-75}$ , Forced expiratory flow between 25% and 75% of FVC;  $FEV_1$ , forced expiratory volume in 1 second; FRC, functional residual capacity; FVC, forced vital capacity; PEFR, peak expiratory flow rate; RV, residual volume; TLC, total lung capacity.

## V. APPARENT LIFE-THREATENING EVENT (ALTE) <sup>12,13</sup>

**Definition:** Events that are frightening to the observer and include some combination of obstructive or central apnea, color change (usually cyanosis and/or pallor), marked change in muscle tone (usually limpness), choking, or gagging. In some cases the observer fears the infant has died or would have died without significant intervention.

Preterm infants (<37 weeks' gestational age) are at increased risk for ALTE given their immature respiratory centers.<sup>14</sup>

### A. Differential Diagnosis (Box 24-1)

In almost half of all cases of ALTEs, no cause is found.<sup>14</sup> The three most common comorbid conditions (which account for roughly 50% of all diagnoses eventually made) are gastroesophageal reflux (GER), seizure, and lower respiratory tract infection.<sup>14</sup>

#### BOX 24-1

##### DIFFERENTIAL DIAGNOSIS OF APPARENT LIFE-THREATENING EVENT

###### I. GASTROENTEROLOGIC

Gastroesophageal reflux disease  
Gastroenteritis  
Esophageal dysfunction  
Surgical abdomen  
Dysphagia

###### II. NEUROLOGIC

Seizure  
Central apnea/hypoventilation  
Meningitis/encephalitis  
Hydrocephalus  
Brain tumor  
Neuromuscular disorders  
Vasovagal reaction

###### III. RESPIRATORY

Respiratory syncytial virus  
Pertussis  
Aspiration  
Respiratory tract infection  
Reactive airway disease  
Foreign body

###### IV. OTOLARYNGOLOGIC

Laryngomalacia  
Subglottic and/or laryngeal stenosis  
Obstructive sleep apnea

**V. CARDIOVASCULAR**

Congenital heart disease  
 Cardiomyopathy  
 Cardiac arrhythmias/prolonged QT syndrome  
 Myocarditis

**VI. METABOLIC/ENDOCRINE**

Inborn error of metabolism  
 Hypoglycemia  
 Electrolyte disturbance

**VII. INFECTIOUS**

Sepsis  
 Urinary tract infection

**VIII. OTHER DIAGNOSIS**

Child maltreatment  
 Shaken baby syndrome  
 Breath-holding spell  
 Choking  
 Drug or toxin reaction  
 Anemia  
 Periodic breathing  
 Factitious disorder imposed by another (Munchausen syndrome by proxy)

Modified from DeWolfe CC. Apparent life-threatening event: a review. *Pediatr Clin North Am.* 2005;52:4.

**B. Workup**

The clinical history and physical exam guide the workup. Treatment should be tailored to diagnosis and prevention of further events.

1. **If history and physical suggest a significant event took place**, consider obtaining a complete blood cell count (signs of infection or anemia), C-reactive protein, urinalysis, arterial blood gas (acid-base status and oxygenation), blood glucose (hypoglycemia), electrocardiogram (ECG [QT interval]), electrolytes, and potentially pertussis, respiratory syncytial virus (RSV), or other viral studies, depending on prevalence.<sup>14</sup>
2. **Further evaluations should be dictated by clinical picture, but some common studies are:**
  - a. Chest radiograph: Pneumonia, bronchiolitis, screen for cardiac disease
  - b. Cardiopulmonary monitoring and/or polysomnography: Continuous assessment of oxygenation and ventilation (especially for recurrent events or unusual apnea), rule out obstructive apnea
  - c. Barium swallow  $\pm$  pH probe: Dysfunctional swallow, GER
  - d. Electroencephalography (EEG): Seizure disorder
  - e. Evaluation for non-accidental trauma, including head computed tomography (CT) if the history and physical raise concern
  - f. Urine toxicology: If suspicious of ingestion

## VI. ASTHMA<sup>15</sup>

A chronic inflammatory disorder of the airways resulting in recurrent episodes of wheezing, breathlessness, chest tightness, and cough, particularly at night and in the early morning. These episodes are usually associated with obstruction of airflow in the lower airway and are reversible either spontaneously or with therapy. The inflammation causes increased airway hyperreactivity to a variety of stimuli: Viral infections, cold air, exercise, emotions, and environmental allergens and pollutants.

### A. Clinical Manifestations

1. **Cough**, increased work of breathing (tachypnea, retractions, or accessory muscle use), wheezing, hypoxia, and hypoventilation. Crackles may also be present with asthma exacerbations.
2. **No audible wheezing** may indicate very poor air movement and severe bronchospasm.
3. **Chest radiographs** often show peribronchial thickening, hyperinflation, and patchy atelectasis.
  - a. If persistent radiographic abnormalities, consider right middle lobe syndrome.

### B. Management

1. **Acute management and status asthmaticus**; see Chapter 1
2. **Initial classification and initiation of treatment** for ages 0–4, 5–11, and ≥12 years: [Figures 24-5, 24-6, and 24-7](#)
3. **Stepwise approach to continued management** for ages 0–4, 5–11, and ≥12 years: [Figures 24-8, 24-9, and 24-10](#)

### C. Prevention of Exacerbations

1. **Ensure up-to-date immunizations**, including influenza.
2. **Create an asthma action plan**  
(<http://www.nhlbi.nih.gov/health/public/lung/index.htm#asthma> or [http://fha.maryland.gov/pdf/mch/Asthma\\_Action\\_Plan.pdf](http://fha.maryland.gov/pdf/mch/Asthma_Action_Plan.pdf)).
3. **Identify and minimize asthma triggers and environmental exposures**, including tobacco smoke, mold, pollen, dust mites, etc.
4. **Assess** symptom control, inhaler technique, and medication adherence with regular clinical evaluations.
  - a. Consider specialist referral for formal pulmonary function test (PFT), monitoring, and allergy testing.
  - b. For dosing guidelines on inhaled corticosteroids, please see [Table EC 24-A](#) on Expert Consult.



TABLE EC 24-A

## ESTIMATED COMPARATIVE DAILY DOSAGES FOR INHALED CORTICOSTEROIDS

Inhaled Corticosteroids (ICS)	Strength	<12 years old			>12 years old		
		Low Dose	Medium Dose	High Dose	Low Dose	Medium Dose	High Dose
Beclomethasone/QVar MDI	40 mcg	2–4 puffs/day	5–8 puffs/day	>8 puffs/day	2–6 puffs/day	7–12 puffs/day	>12 puffs/day
	80 mcg	1–2 puffs/day	3–4 puffs/day	>4 puffs/day	1–3 puffs/day	3–6 puffs/day	>6 puffs/day
Budesonide/Pulmicort DPI Flexhaler	90 mcg	2–4 puffs/day	4–8 puffs/day	>8 puffs/day	2–6 puffs/day	7–12 puffs/day	>12 puffs/day
	180 mcg	1–2 puffs/day	2–4 puffs/day	>4 puffs/day	1–3 puffs/day	4–6 puffs/day	>6 puffs/day
Ciclesonide	80 mcg/actuation	See Formulary remarks for ciclesonide			1 puff BID	2 puffs BID	4 puffs BID
	160 mcg/actuation	See Formulary remarks for ciclesonide			N/A	1 puff BID	2 puffs BID
Budesonide/Pulmicort Respule	0.25 mg neb	2 nebs/day	4 nebs/day	8 nebs/day	N/A	N/A	N/A
	0.5 mg neb	1 neb/day	2 nebs/day	4 nebs/day	N/A	N/A	N/A
Flunisolide/Aerospan MDI	80 mcg	2 puffs/day	4 puffs/day	>8 puffs/day	4 puffs/day	5–8 puffs/day	>8 puffs/day
	250 mcg	2–3 puffs/day	4–5 puffs/day	>5 puffs/day	2–4 puffs/day	5–8 puffs/day	>8 puffs/day
Fluticasone/Flovent MDI	44 mcg	2–4 puffs/day	5–8 puffs/day	>8 puffs/day	2–6 puffs/day	7–10 puffs/day	>10 puffs/day
	110 mcg	1 puff/day	2–3 puffs/day	>3 puffs/day	1–2 puffs/day	3–4 puffs/day	>4 puffs/day
	220 mcg	N/A	1 puff/day	>1 puff/day	1 puff/day	2 puffs/day	>2 puffs/day
Fluticasone/Flovent Diskus DPI	50 mcg	2–4 puffs/day	5–8 puffs/day	>8 puffs/day	2–6 puffs/day	7–10 puffs/day	>10 puffs/day
	100 mcg	1–2 puffs/day	2–4 puffs/day	>4 puffs/day	1–3 puffs/day	4–5 puffs/day	>5 puffs/day
	250 mcg	N/A	1 puff/day	>1 puff/day	1 puff/day	2 puffs/day	>2 puffs/day
Mometasone/Asmanex Twisthaler	220 mcg	N/A	N/A	N/A	1 puff	2 puffs	>2 puffs

Continued

TABLE EC 24-A

## ESTIMATED COMPARATIVE DAILY DOSAGES FOR INHALED CORTICOSTEROIDS (Continued)

Inhaled Corticosteroids (ICS)	Strength		<12 years old			>12 years old	
COMBINATION DRUGS: ICS + LABA*							
Fluticasone/Salmeterol MDI (Advair)	45/21 mcg	2 puffs/day	2–3 puffs/day	4 puffs/day	2 puffs/day	3–4 puffs/day	
	115/21 mcg		2 puffs/day	2–4 puffs/day	2 puffs/day	2 puffs/day	3–4 puffs/day
	230/21 mcg			2–4 puffs/day			3–4 puffs/day
Fluticasone/Salmeterol Diskus DPI (Advair)	100/50 mcg	1 puff/day	2 puffs/day	2 puffs/day		2 puffs/day	
	250/50 mcg			2 puffs/day		1 puff/day	2 puffs/day
	500/50 mcg			2 puffs/day			2 puffs/day
Budesonide/Formoterol (Symbicort)	80/4.5 mcg MDI	1–2 puffs/day	2–4 puffs/day		1–3 puffs/day	4 puffs/day	
	160/4.5 mcg MDI		1–2 puffs/day	2–4 puffs/day		2 puffs/ day	4 puffs/day
Mometasone/Formoterol (Dulera)	100 mcg mometasone + 5 mcg formoterol	No dosing information currently available for <12 yo			N/A	2 puffs BID	N/A
	200 mcg mometasone + 5 mcg formoterol	No dosing information currently available for <12 yo			N/A	N/A	2 puffs BID

\*For ICS + LABA combination drugs, patient should not take more than 2 puffs per dose of the MDI, 1 puff per dose of the DPI, or 2 doses per day.

DPI, Dry powder inhaler; ICS, inhaled corticosteroid; LABA, long-acting  $\beta$ -agonist; LTRA, leukotriene receptor antagonist; MDI metered-dose inhaler.

Modified from Expert Panel Report III. Guidelines for the diagnosis and management of asthma—full report 2007; National Institutes of Health Pub. No. 08-4051. Bethesda, MD: National Asthma Education and Prevention Program, 2007.

## CLASSIFYING ASTHMA SEVERITY AND INITIATING TREATMENT IN CHILDREN 0–4 YEARS OF AGE

Assessing severity and initiating therapy in children who are not currently taking long-term control medication

Components of severity		Classification of asthma severity (0–4 years of age)			
		Intermittent	Persistent		
			Mild	Moderate	Severe
Impairment	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	0	1–2×/month	3–4×/month	>1×/week
	Short-acting beta <sub>2</sub> -agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not daily	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year	≥2 exacerbations in 6 months requiring oral systemic corticosteroids, or ≥4 wheezing episodes/1 year lasting >1 day AND risk factors for persistent asthma		
		Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time. Exacerbations of any severity may occur in patients in any severity category.			
Recommended step for initiating therapy  (See Fig. 24-8 for treatment steps.)		Step 1	Step 2	Step 3 and consider short course of oral systemic corticosteroids	
		In 2–6 weeks, depending on severity, evaluate level of asthma control that is achieved. If no clear benefit is observed in 4–6 weeks, consider adjusting therapy or alternative diagnoses.			

Key: EIB, exercise-induced bronchospasm

### Notes

- The stepwise approach is meant to assist, not replace, the clinical decision making required to meet individual patient needs.
- Level of severity is determined by both impairment and risk. Assess impairment domain by patient's/caregiver's recall of previous 2–4 weeks. Symptom assessment for longer periods should reflect a global assessment such as inquiring whether the patient's asthma is better or worse since the last visit. Assign severity to the most severe category in which any feature occurs.
- At present, there are inadequate data to correspond frequencies of exacerbations with different levels of asthma severity. For treatment purposes, patients who had ≥2 exacerbations requiring oral systemic corticosteroids in the past 6 months, or ≥4 wheezing episodes in the past year, and who have risk factors for persistent asthma may be considered the same as patients who have persistent asthma, even in the absence of impairment levels consistent with persistent asthma.

**FIGURE 24-5**

Guidelines for classifying asthma severity and initiating treatment in infants and young children (0–4 years of age). (Adapted from NAEPP—Expert Panel Report 3. Guidelines for the Diagnosis and Management of Asthma, August 2007. <http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm>.)

## CLASSIFYING ASTHMA SEVERITY AND INITIATING TREATMENT IN CHILDREN 5–11 YEARS OF AGE

Assessing severity and initiating therapy in children who are not currently taking long-term control medication

Components of severity		Classification of asthma severity (5–11 years of age)			
		Intermittent	Persistent		
			Mild	Moderate	Severe
Impairment	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2×/month	3–4×/month	>1×/week but not nightly	Often 7×/week
	Short-acting beta <sub>2</sub> -agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not daily	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung function	• Normal FEV <sub>1</sub> between exacerbations • FEV <sub>1</sub> >80% predicted • FEV <sub>1</sub> /FVC >85%	• FEV <sub>1</sub> = >80% predicted • FEV <sub>1</sub> /FVC >80%	• FEV <sub>1</sub> = 60%–80% predicted • FEV <sub>1</sub> /FVC = 75%–80%	• FEV <sub>1</sub> <60% predicted • FEV <sub>1</sub> /FVC <75%
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year (see note)	≥2/year (see note) →		
		← Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time → for patients in any severity category.			
		Relative annual risk of exacerbations may be related to FEV <sub>1</sub> .			
Recommended step for initiating therapy  (See Fig. 24-9 for treatment steps.)		Step 1	Step 2	Step 3, medium-dose ICS option	Step 3, medium-dose ICS option, or step 4
		and consider short course of oral systemic corticosteroids			
		In 2–6 weeks, evaluate level of asthma control that is achieved, and adjust therapy accordingly.			

Key: EIB, exercise-induced bronchospasm; FEV<sub>1</sub>, forced expiratory volume in 1 second; FVC, forced vital capacity; ICS, inhaled corticosteroids

### Notes

- The stepwise approach is meant to assist, not replace, the clinical decision making required to meet individual patient needs.
- Level of severity is determined by both impairment and risk. Assess impairment domain by patient's/caregiver's recall of previous 2–4 weeks and spirometry. Assign severity to the most severe category in which any feature occurs.
- At present, there are inadequate data to correspond frequencies of exacerbations with different levels of asthma severity. In general, more frequent and intense exacerbations (e.g., requiring urgent, unscheduled care, hospitalization, or ICU admission) indicate greater underlying disease severity. For treatment purposes, patients who had ≥2 exacerbations requiring oral systemic corticosteroids in the past year may be considered the same as patients who have persistent asthma, even in the absence of impairment levels consistent with persistent asthma.

### FIGURE 24-6

Guidelines for classifying asthma severity and initiating treatment in children 5–11 years of age. (Adapted from NAEP—Expert Panel Report 3. *Guidelines for the Diagnosis and Management of Asthma*, August 2007. <http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm>.)

## CLASSIFYING ASTHMA SEVERITY AND INITIATING TREATMENT IN YOUTHS ≥12 YEARS OF AGE

Assessing severity and initiating treatment for patients who are not currently taking long-term control medications

Components of severity		Classification of asthma severity ≥12 years of age			
		Intermittent	Persistent		
			Mild	Moderate	Severe
Impairment  Normal FEV <sub>1</sub> /FVC: 8–19 yr 85% 20–39 yr 80% 40–59 yr 75% 60–80 yr 70%	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2×/month	3–4×/month	>1×/week but not nightly	Often 7×/week
	Short-acting beta <sub>2</sub> -agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not daily, and not more than 1 time on any day	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung function	• Normal FEV <sub>1</sub> between exacerbations • FEV <sub>1</sub> >80% predicted  • FEV <sub>1</sub> /FVC normal	• FEV <sub>1</sub> >80% predicted • FEV <sub>1</sub> /FVC normal	• FEV <sub>1</sub> >60% but <80% predicted • FEV <sub>1</sub> /FVC reduced 5%	• FEV <sub>1</sub> <60% predicted • FEV <sub>1</sub> /FVC reduced >5%
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year (see note)	≥2/year (see note) →		
		Consider severity and interval since last exacerbation. ← Frequency and severity may fluctuate over time → for patients in any severity category.			
		Relative annual risk of exacerbations may be related to FEV <sub>1</sub> .			
Recommended step for initiating treatment  (See Fig. 24-10 for treatment steps.)		Step 1	Step 2	Step 3	Step 4 or 5
		and consider short course of oral systemic corticosteroids			
		In 2–6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly.			

Key: FEV<sub>1</sub>, forced expiratory volume in 1 second; FVC, forced vital capacity; ICU, intensive care unit

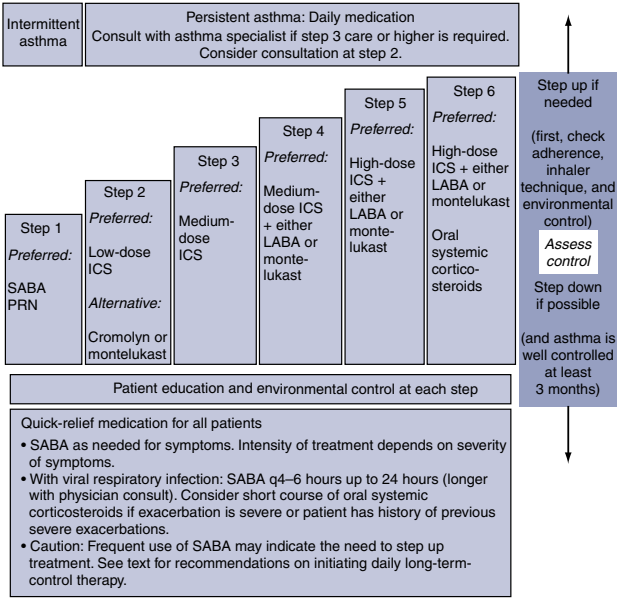
### Notes

- The stepwise approach is meant to assist, not replace, the clinical decision making required to meet individual patient needs.
- Level of severity is determined by both impairment and risk. Assess impairment domain by patient's/caregiver's recall of previous 2–4 weeks and spirometry. Assign severity to the most severe category in which any feature occurs.
- At present, there are inadequate data to correspond frequencies of exacerbations with different levels of asthma severity. In general, more frequent and intense exacerbations (e.g., requiring urgent, unscheduled care, hospitalization, or ICU admission) indicate greater underlying disease severity. For treatment purposes, patients who had ≥2 exacerbations requiring oral systemic corticosteroids in the past year may be considered the same as patients who have persistent asthma, even in the absence of impairment levels consistent with persistent asthma.

**FIGURE 24-7**

Guidelines for classifying asthma severity and initiating treatment in youth 12 and older. (Adapted from NAEPP—Expert Panel Report 3. *Guidelines for the Diagnosis and Management of Asthma*, August 2007. <http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm>.)

**STEPWISE APPROACH FOR MANAGING ASTHMA IN CHILDREN 0-4 YEARS OF AGE**



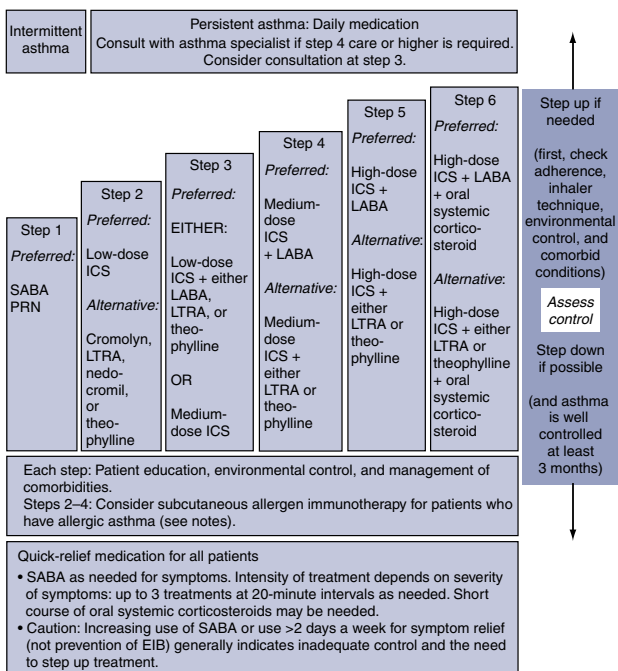
**Key:** **Alphabetical order is used when more than one treatment option is listed within either preferred or alternative therapy.** ICS, inhaled corticosteroid; LABA, long-acting inhaled beta<sub>2</sub>-agonist; SABA, short-acting inhaled beta<sub>2</sub>-agonist

- Notes:**
- The stepwise approach is meant to assist, not replace, the clinical decision making required to meet individual patient needs.
  - If alternative treatment is used and response is inadequate, discontinue it and use the preferred treatment before stepping up.
  - If clear benefit is not observed within 4–6 weeks and patient/family medication technique and adherence are satisfactory, consider adjusting therapy or alternative diagnosis.
  - Studies on children 0–4 years of age are limited. Step 2 preferred therapy is based on Evidence A. All other recommendations are based on expert opinion and extrapolation from studies in older children.

**FIGURE 24-8**

Stepwise approach for managing asthma in infants and young children (0–4 years of age). (Adapted from NAEPP—Expert Panel Report 3. *Guidelines for the Diagnosis and Management of Asthma*, August 2007. <http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm>.)

## STEPWISE APPROACH FOR MANAGING ASTHMA IN CHILDREN 5–11 YEARS OF AGE



**Key:** Alphabetical order is used when more than one treatment option is listed within either preferred or alternative therapy. ICS, inhaled corticosteroid; LABA, long-acting inhaled beta<sub>2</sub>-agonist; LTRA, leukotriene receptor antagonist; SABA, short-acting inhaled beta<sub>2</sub>-agonist

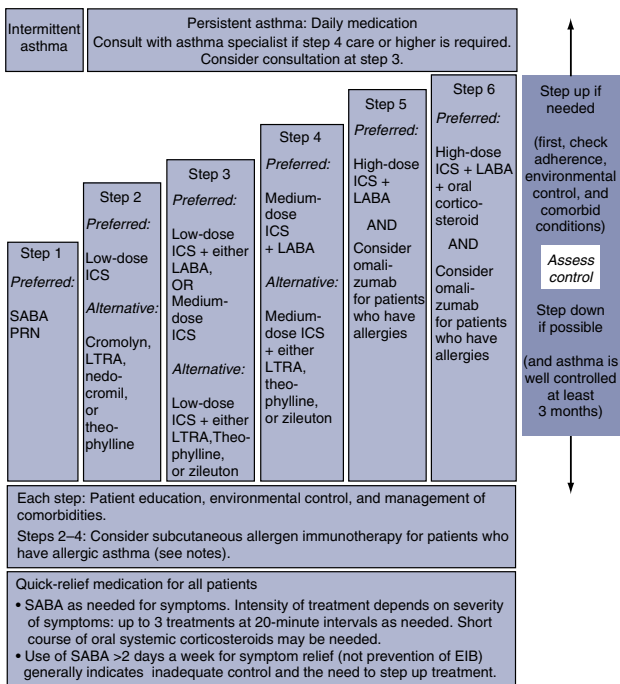
### Notes:

- The stepwise approach is meant to assist, not replace, the clinical decision making required to meet individual patient needs.
- If alternative treatment is used and response is inadequate, discontinue it and use the preferred treatment before stepping up.
- Theophylline is a less desirable alternative due to the need to monitor serum concentration levels.
- Step 1 and step 2 medications are based on Evidence A. Step 3 ICS + adjunctive therapy and ICS are based on Evidence B for efficacy of each treatment and extrapolation from comparator trials in older children and adults—comparator trials are not available for this age group; steps 4–6 are based on expert opinion and extrapolation from studies in older children and adults.
- Immunotherapy for steps 2–4 is based on Evidence B for house-dust mites, animal danders, and pollens; evidence is weak or lacking for molds and cockroaches. Evidence is strongest for immunotherapy with single allergens. The role of allergy in asthma is greater in children than in adults. Clinicians who administer immunotherapy should be prepared and equipped to identify and treat anaphylaxis that may occur.

**FIGURE 24-9**

Stepwise approach for managing asthma in children 5–11. (Adapted from NAEPP—Expert Panel Report 3. *Guidelines for the Diagnosis and Management of Asthma*, August 2007. <http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm>.)

## STEPWISE APPROACH FOR MANAGING ASTHMA IN YOUTH ≥12 YEARS OF AGE AND ADULTS



Key: Alphabetical order is used when more than one treatment option is listed within either preferred or alternative therapy. EIB, exercise-induced bronchospasm; ICS, inhaled corticosteroid; LABA, long-acting inhaled  $\beta_2$ -agonist; LTRA, leukotriene receptor antagonist; PRN, as needed; SABA, shortacting inhaled  $\beta_2$ -agonist

### Notes:

- The stepwise approach is meant to assist, not replace, the clinical decision making required to meet individual patient needs.
- If alternative treatment is used and response is inadequate, discontinue it and use the preferred treatment before stepping up.
- Zileuton is a less-desirable alternative due to limited studies as adjunctive therapy and the need to monitor liver function. Theophylline requires monitoring of serum concentration levels.
- In step 6, before oral systemic corticosteroids are introduced, a trial of high-dose ICS + LABA + either LTRA, theophylline, or zileuton may be considered, although this approach has not been studied in clinical trials.
- Step 1, 2, and 3 preferred therapies are based on Evidence A; step 3 alternative therapy is based on Evidence A for LTRA, Evidence B for theophylline, and Evidence D for zileuton. Step 4 preferred therapy is based on Evidence B, and alternative therapy is based on Evidence B for LTRA and theophylline and Evidence D for zileuton. Step 5 preferred therapy is based on Evidence B. Step 6 preferred therapy is based on Expert Panel Report 2 (1997) and Evidence B for omalizumab.
- Immunotherapy for steps 2–4 is based on Evidence B for house-dust mites, animal danders, and pollens; evidence is weak or lacking for molds and cockroaches. Evidence is strongest for immunotherapy with single allergens. The role of allergy in asthma is greater in children than in adults.
- Clinicians who administer immunotherapy or omalizumab should be prepared and equipped to identify and treat anaphylaxis that may occur.

**FIGURE 24-10**

Stepwise approach for managing asthma in youth 12 and older. (Adapted from NAEPP—Expert Panel Report 3. Guidelines for the Diagnosis and Management of Asthma, August 2007. <http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm>.)



## VII. BRONCHIOLITIS<sup>16</sup>

Bronchiolitis is a lower respiratory tract infection common in infants and children 2 years of age and younger. It is characterized by acute inflammation, edema, and necrosis of airway epithelium, leading to increased mucus production and bronchospasm. It is most commonly caused by RSV, but can also be seen with other viruses including: parainfluenza, adenovirus, mycoplasma, and human metapneumovirus.

### A. Clinical Manifestations

1. **Variable and dynamic course** ranging from transient apnea and mucus plugging to progressive lower airway disease
  - a. Initial symptoms: Clear rhinorrhea, diminished appetite, fever, cough
  - b. Later symptoms: Tachypnea, wheezing, dyspnea, irritability
2. **Radiographic findings:** Hyperinflation and patchy atelectasis

### B. Treatment

Mainstay is supportive care.

1. **Consider hospitalization** based on clinical presentation, need for supplemental oxygen, or inability to feed. Should be strongly considered for patients <12 weeks, history of prematurity, underlying cardiopulmonary disease, or immunodeficiency.
2. **Supplemental oxygen therapy** for consistently low oxygen saturation ( $SpO_2$ ).
  - a. Consider maintaining higher  $SpO_2$  for those with fever, acidosis, or hemoglobinopathies due to oxyhemoglobin desaturation curve, or for increased work of breathing.
3. **A trial of bronchodilators is an option** but should be continued only if there is documented improved clinical response.
4. **Corticosteroids and antibiotics** should not be used routinely in bronchiolitis (unless signs of bacterial co-infection).
5. **Fluid support is often needed** owing to increased losses from tachypnea, fever, and poor oral intake.
  - a. Hold oral feedings in hospitalized infants who are very tachypneic to minimize risk of aspiration.
6. **Consider hypertonic saline nebulizer treatments** in previously healthy infants while they are hospitalized.
  - a. Albuterol is often given with hypertonic saline nebulizer treatments to reduce the bronchospasm induced by hypertonic saline.

### C. Clinical Pearls

1. **In infants younger than 3 months with RSV**, there is an appreciable incidence of co-infection with urinary tract infection (UTI) and/or acute otitis media, but pneumonia is uncommon.<sup>16</sup>
2. **Infants hospitalized for bronchiolitis** are more likely to have recurrent wheezing.
3. **Ensure RSV immunoprophylaxis** for high-risk infants. See Chapter 16.

**VIII. BRONCHOPULMONARY DYSPLASIA (BPD)**<sup>17-19</sup>

Also known as chronic lung disease of prematurity or chronic lung disease of infancy, BPD is a chronic pulmonary condition that usually evolves after premature birth, characterized by the need for oxygen supplementation >21% for at least 28 days after birth. Thought to be a result of airway inflammation, damage from hyperoxia, hypoxia, or mechanical ventilation; results in interference with normal lung alveolar, airway, and vascular development.

**A. Diagnostic Criteria**

1. **Severity based on oxygen requirement** at time of assessment and characterized as mild if on room air, moderate if requiring <30% oxygen, or severe if requiring >30% oxygen and/or positive pressure.
  - a. If gestational age at birth was <32 weeks: Assess infant at 36 weeks' postmenstrual age or at discharge to home, whichever comes first.
  - b. If gestational age at birth >32 weeks: Assess infant at 28–56 days postnatal age or at discharge to home, whichever comes first.

**B. Clinical Manifestations and Management of Established BPD**

1. **Children with BPD** may have persistent respiratory symptoms, airway hyperreactivity, and supplemental oxygen requirements, especially during intercurrent illness. These children often require some combination of the following for their lung disease:
  - a. Bronchodilators.
  - b. Antiinflammatory agents.
  - c. Supplemental oxygen therapy.
  - d. Diuretics.
  - e. Severe cases may require tracheostomy and prolonged mechanical ventilation.
  - f. Remember RSV and flu prophylaxis.
2. **Need close monitoring for complications**, which can affect multiple organ systems besides lungs: Pulmonary or systemic hypertension, electrolyte abnormalities, nephrocalcinosis (from chronic diuretics), neurodevelopmental or growth delay, aspiration from dysphagia and/or GER, and more severe superinfections with RSV or flu.

**IX. CYSTIC FIBROSIS (CF)**<sup>20-22</sup>

An autosomal recessive disorder in which mutations of the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene reduce the function of a chloride channel that usually resides within mucosal epithelial cells in the airways, pancreatic ducts, biliary tree, intestine, vas deferens, and sweat glands. Most patients have chronic progressive obstructive pulmonary disease, pancreatic exocrine insufficiency with protein and fat malabsorption, and abnormally high sweat electrolyte concentrations.

**A. Clinical Manifestations (Table 24-6)****B. Diagnosis**

Over half of patients are diagnosed by 6 months of age, three fourths by 2 years.

TABLE 24-6

## MAJOR CLINICAL MANIFESTATIONS OF CYSTIC FIBROSIS BY ORGAN SYSTEM

Respiratory	Chronic productive cough, hemoptysis Bronchiectasis, bronchitis, pneumonia Sinusitis Nasal polyposis
Gastrointestinal	Meconium ileus Rectal prolapse Pancreatic insufficiency Distal intestinal obstruction syndrome (DIOS) Fat-soluble vitamin deficiency (A, D, E, K) Liver disease including cirrhosis
Genitourinary	Infertility (male) and decreased fertility (female) Absence of vas deferens
Miscellaneous	Increased sweat electrolytes Hypokalemic alkalosis Digital clubbing Pulmonary hypertrophic osteoarthropathy Failure to thrive

- Quantitative pilocarpine ionoelectrophoresis (sweat chloride) test:** Gold standard for diagnosis.
  - Positive for CF:  $>60$  mEq/L (mEq/L = mmol/L)
  - Indeterminant:
    - Infants  $<6$  months: Indeterminant if 30–60 mEq/L
    - Children  $>6$  months: Indeterminant if 40–60 mEq/L
  - Normal:
    - Infants  $<6$  months: Normal if  $<30$  mEq/L
    - Children  $>6$  months: Normal if  $<40$  mEq/L
- DNA testing is becoming increasingly important in diagnosis.** Over 1800 mutations have been described, most common is F508del (present in 70% of those with CF).
- Many states have adopted universal newborn screening (NBS)** by measuring infants' immunoreactive trypsinogen (IRT) levels and/or DNA testing for most common mutations. A confirmatory sweat chloride test should be performed promptly in those patients who have a positive NBS result.
- Clinical pearl:** Elevated sweat chloride levels can be from other disorders, including untreated adrenal insufficiency, glycogen storage disease type 1, fucosidosis, hypothyroidism, nephrogenic diabetes insipidus, ectodermal dysplasia, malnutrition, mucopolysaccharidosis, panhypopituitarism, or poor testing technique.

### C. Pulmonary Therapies

- Airway clearance therapy (ACT)** to mobilize airway secretions and facilitate expectoration: Often manual/mechanical percussion and postural drainage. Older children may use high-frequency chest wall compression device (vest therapy), mechanical chest percussors, or

oscillatory positive expiratory pressure (PEP) handheld devices (e.g., flutter valve and acapella).

2. **Aerosolized medications** to increase mucociliary clearance: recombinant human DNAase (dornase alfa), which cleaves nucleic material, and hypertonic saline nebs to hydrate airway mucus and stimulate cough
3. **Chronic antibiotics:** If *Pseudomonas aeruginosa* is persistently present in culture of airways, consider aerosolized aminoglycosides and/or chronic oral macrolide therapy.
4. **Intermittent use of IV antibiotics** when hospitalized for exacerbations. Common bacteria that cause exacerbations include *P. aeruginosa* and *Staphylococcus aureus*.

## D. Management of Common CF Complications

### 1. Pancreatic disease

- a. Pancreatic enzyme replacement therapy (PERT) prior to meals to improve digestion and intestinal absorption of dietary protein and fat
- b. Nutritional supplementation to maintain body mass index (BMI)  $\geq 50$ th percentile
- c. Monitoring for CF-induced diabetes or liver disease

### 2. Infertility:

- a. Absence of the vas deferens; however, assisted fertilization is possible using aspiration of viable sperm from testes
- b. Women may have trouble becoming pregnant because of mucus-associated obstruction of the cervix.
3. **Decreased life expectancy;** survival continues to improve, and median predicted survival age is over 37 years.

## X. OBSTRUCTIVE SLEEP APNEA SYNDROME (OSAS) 23-38

Part of the spectrum of sleep-disordered breathing; characterized by prolonged partial and/or intermittent partial or complete upper airway obstruction with accompanying hypoxemia, hypercapnia, and/or sleep disruption. Alternate names include *obstructive hypoventilation*, *upper airway resistance syndrome*.

### A. Clinical Manifestations

1. **Snoring** sometimes accompanied by snorts, gasps, or intermittent pauses in breathing.
2. **Increased respiratory effort** during sleep, disturbed or restless sleep with increased arousals and awakenings.
3. **Daytime cognitive and/or behavioral problems.** (Young children rarely present with daytime sleepiness.)
4. **Long-term complications** include neurocognitive impairment, behavioral problems, poor growth, and systemic and pulmonary hypertension.
5. **Risk factors include** adenotonsillar hypertrophy, obesity, family history of OSAS, craniofacial or laryngeal anomalies, prematurity, nasal/pharyngeal inflammation, cerebral palsy, and neuromuscular disease.

## B. Diagnosis

1. **Screen for snoring** during routine well-child care.
2. **If a child snores on a regular basis** and has any of the complaints or findings shown in [Box 24-2](#), clinicians should either (1) obtain a polysomnogram OR (2) refer the patient to a sleep specialist or otolaryngologist for more extensive evaluation.<sup>23</sup>
  - a. Polysomnography includes measurement of EEG, electrooculography (EOG), and electromyography (EMG) to monitor sleep stage and movement; ECG; chest wall and abdominal movement to assess respiratory effort; nasal/oral airflow; and transcutaneous or ETco<sub>2</sub> (ventilation) and pulse oximetry (oxygenation).
  - b. Diagnosis of OSAS by polysomnography is based on obstructive apnea-hypopnea index (AHI) and gas exchange abnormalities resulting from upper airway obstruction. Polysomnography is used to differentiate OSAS from benign snoring and other disorders that may disrupt sleep, including central hypoventilation syndrome, sleep-related respiratory failure related to neuromuscular or lung disease, and nocturnal seizures.

## C. Treatment

1. **Tonsillectomy and adenoidectomy** are mainstays of treatment.
2. **Continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP)** for patients who fail surgical therapy or are not candidates for surgery.

### BOX 24-2

#### SYMPTOMS AND SIGNS OF OSAS

##### I. HISTORY

Frequent snoring ( $\geq 3$  nights/week)  
 Labored breathing during sleep  
 Gasping/snorting noises or observed episodes of apnea  
 Sleep enuresis (especially secondary enuresis)  
 Sleeping in a seated position or with the neck hyperextended  
 Cyanosis  
 Headache on awakening  
 Daytime sleepiness  
 Attention-deficit/hyperactivity disorder  
 Learning problems

##### II. PHYSICAL EXAM

Underweight or overweight  
 Tonsillar hypertrophy  
 Adenoidal facies  
 Micrognathia/retrognathia  
 High-arched palate  
 Failure to thrive  
 Hypertension

Adapted from Marcus CL, Brooks LJ, Draper KA, et al. Diagnosis and management of childhood obstructive sleep apnea syndrome. *Pediatrics*. 2012;130:575-584.

3. **Weight loss in obese children.**
4. **Treatment of upper respiratory allergies.**

### XI. SUDDEN INFANT DEATH SYNDROME<sup>27</sup>

Sudden death of an infant younger than 1 year that remains unexplained after a thorough case investigation, including performance of complete autopsy, examination of death scene, and review of clinical history. Thought to be caused when a genetically vulnerable infant is exposed to an exogenous stressor during a critical developmental period when there is immaturity of the cardiorespiratory system, autonomic nervous system, immune system, and arousal pathways, together with a failure of arousal responsiveness from sleep.

#### A. Epidemiology

1. **Incidence is** 0.56 per 1000 in the United States, 2–3 times higher in African American and Native American populations.
2. **Peak incidence is** at 2–4 months of age, with male predominance.

#### B. Risk Factors and Protective Factors (Box 24-3)

##### BOX 24-3

##### FACTORS ASSOCIATED WITH SUDDEN INFANT DEATH SYNDROME (SIDS)

###### Risk Factors

Premature birth  
In utero and postnatal smoke exposure  
Side and prone sleeping  
Sleeping on soft mattress and bedding  
Overbundling  
Bed sharing  
Recent infection  
Siblings with SIDS  
Low socioeconomic factors

###### Protective Factors

Sleeping in supine position  
Sleeping on firm mattress  
Pacifier use during sleep  
Live and sleep in smoke-free zone  
Sleep in same room as caregivers  
Breastfeeding

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# Chapter 25

## Radiology

Jessica Knight-Perry, MD

### I. GENERAL PEDIATRIC PRINCIPLES

The amount of radiation children receive from medical sources is increasing. Considerations unique to the pediatric population are greater radiosensitivity of the thyroid gland, breast tissue, and gonads. Compared to adults, children have a longer lifespan in which to manifest radiation-related cancer. One computed tomography (CT) scan of the chest, for example, is equivalent to about 68 chest x-rays.<sup>1</sup>

#### A. Employ Judicious Use of CT

**Consider ultrasound (US) or magnetic resonance imaging (MRI) whenever possible.** If CT is indicated, remember the following to help minimize radiation exposure

1. **To limit exposure**, decrease tube voltage (kVp) and tube current (mA) through the development of child-size protocols.
2. **One scan (single phase) is often enough.**
3. **Scan only the indicated areas** (e.g., do not include pelvis if only abdomen is needed).
4. **Body CT scans without intravenous (IV) contrast are helpful** in delineating fine bony detail, calcifications, and lung parenchyma, but almost nothing else. If your clinical question concerns something other than these areas, and you cannot use IV contrast, then consider ultrasound as a substitute for CT.
5. For further information regarding appropriate use of radiation for the pediatric patient, please refer to [www.imagegently.org](http://www.imagegently.org).

### II. HEAD

Most intracranial processes, malformations, and tumors are best imaged with MRI. MRI is useful for neurodegenerative and demyelination disorders, diffuse axonal injury, neurocutaneous syndromes, structural lesions in focal seizure disorders, and vascular lesions. Compared to CT, MRI is more useful in detecting lesions in the posterior fossa.

#### A. Germinal Matrix Hemorrhage

Premature infants should undergo head US to detect intraventricular hemorrhage and periventricular leukomalacia and to screen for hydrocephalus and congenital abnormalities.

#### B. Congenital Malformations

Once detected on US, malformations are best further defined with MRI.

#### C. Congenital Infections

1. **Congenital infections such as herpes simplex virus (HSV) are best imaged with MRI.**



2. **Calcifications consistent with toxoplasmosis and cytomegalovirus (CMV) infection may be best detected with CT.** Calcifications in toxoplasmosis have a predilection for the basal ganglia and tend to be more diffuse than those of CMV, which primarily affects the periventricular region.

#### D. Head Trauma

1. **Best imaged by noncontrast CT to reveal skull fractures and subdural and epidural hematomas.** A head CT should be part of a physical abuse workup.
2. **Skull radiography is of limited value.**
3. **Multiple hemorrhages of various ages are best detected with MRI.**

#### E. Ventriculoperitoneal (VP) Shunt Malfunction

Initial imaging includes head CT to determine ventricle size. If signs of shunt malfunction are noted, radiographs of the length of the shunt (a shunt series) should follow to look for kinks or disconnections.

#### F. Craniosynostosis

Suture examination is best done initially with radiographs of the skull. If there are changes consistent with craniosynostosis, three-dimensional CT reconstructions should be obtained.

### III. EYES

#### A. Orbital Cellulitis (Fig. 25-1)

1. **Best imaged with contrast CT with orbital cuts.**
2. **To determine whether an infection is preseptal or postseptal,** a line is drawn from the medial to the lateral bony walls of the orbit on transverse cuts.

### IV. SPINE

#### A. Cervical Spine Trauma<sup>3,4</sup>

1. **After immobilization in a collar,** lateral and anteroposterior (AP) radiographs of the cervical spine (C-spine) should be performed in all children who have sustained significant head trauma, deceleration injury, or undergone unwitnessed trauma. The C7 vertebral body and the C7–T1 junction must be visualized. C-spine injuries are most common from the occiput to C3 in children (especially subluxation at the atlanto-occipital joint or atlantoaxial joint in infants and toddlers) and in the lower C-spine in older children and adults.
2. **Flexion-extension films may be helpful,** especially in patients with Down syndrome, who are at risk for atlantoaxial subluxation.
3. **Odontoid views may be helpful in older children with suspected occipito-cervical injury** (e.g., whiplash).

#### B. Reading C-spine Films<sup>3,4</sup>

The following ABCDDS (or ABCDs) mnemonic is useful:

1. **Alignment:** Anterior vertebral body line, posterior vertebral body line, facet line, and spinous process line should each form a continuous line with smooth contour and no step-offs (Fig. 25-2).

**FIGURE 25-1**

Orbital cellulitis with subperiosteal abscess. Preseptal and extracoronar portions of the medial right orbit are involved. Medial rectus muscle is slightly thickened and displaced, and a small focal fluid collection (*arrow*) representing a subperiosteal abscess is present. (From Slovis TL. Caffey's Pediatric Diagnostic Imaging. 11th ed. Philadelphia: Mosby, 2008. Courtesy Kenneth D. Hopper, MD, Hershey, Pa.)

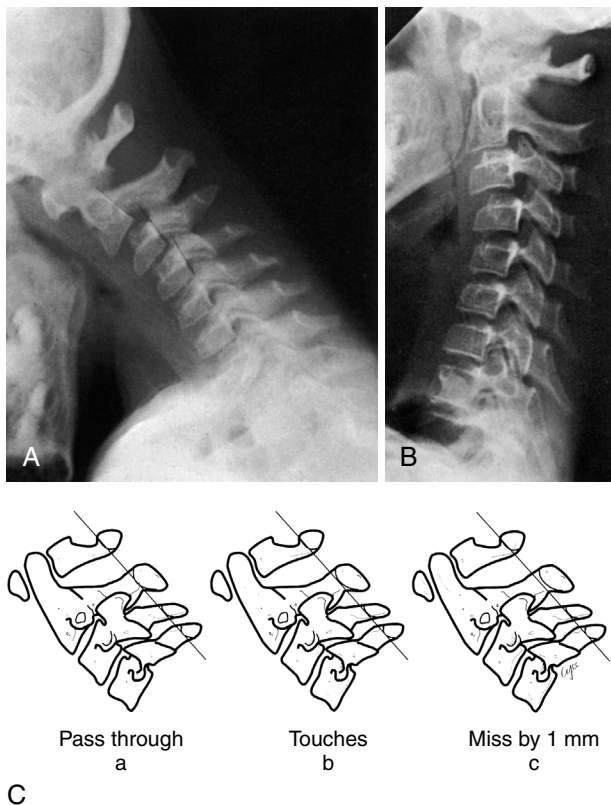
2. **Bones:** Assess each bone looking for chips or fractures.
3. **Count:** Must see C7 body in its entirety.
4. **Dens:** Examine for chips or fractures.
5. **Disk spaces:** Should see consistent distance between each vertebral body.
6. **Soft tissue:** Assess for swelling, particularly in prevertebral area.

#### **C. Spinal Cord Injury without Radiographic Abnormality (SCIWORA)<sup>4,5</sup>**

1. **Definition:** A functional C-spine injury that cannot be excluded by abnormality on a radiograph; thought to be attributable to the increased mobility of a child's spine.
2. **Should be suspected in the setting of normal C-spine images when** clinical signs or symptoms (e.g., point tenderness, focal neurologic symptoms) suggest C-spine injury.
3. **If neurologic symptoms persist despite normal C-spine and flexion-extension views,** MRI is indicated to rule out swelling, contusion, or intramedullary hemorrhage of the cord.

#### **D. Spinal Dysraphism (e.g., myelocoele, myelomeningocele)**

Initial imaging: Radiographs. Most often screened for with US. Abnormalities are followed by MRI.

**FIGURE 25-2**

Normal cervical spine mobility in children. **A**, Normal forward shift of C2 on C3 in an asymptomatic 3-year-old girl. **B**, Normal forward shift of C3 on C4 (pseudosubluxation) in an asymptomatic 5-year-old girl. **C**, Normal limits of the posterior cervical line. Normal posterior cervical line can pass through or just behind the anterior cortex of C2 (a), touch the anterior cortex of C2 (b), or come within 1 mm of the anterior aspect of C2 (c). (**A** and **B** from Sullivan CR, Bruwer AJ, Harris LE. *Hypermobility of the cervical spine in children: a pitfall in the diagnosis of cervical dislocation*. *Am J Surg*. 1958;95:636-640; **C** from Kuhns LR. *Imaging of Spinal Trauma in Children: An Atlas and Text*. Hamilton Ontario: BC Decker, 1998:31.)

**E. Scoliosis**

Best evaluated by erect AP spine radiograph. Posteroanterior (PA) views can be used in postpubertal girls to decrease breast radiation dose.

**V. AIRWAY**

**A. Lateral Radiograph**

1. **Lateral radiograph of the upper airway is the most useful film for evaluating a child with stridor.** If possible, should be obtained on inspiration.
2. **A radiologic workup should always include AP and lateral radiographs of the chest,** with inclusion of upper airway on the AP view. Diagnosis is based on airway radiologic examination in conjunction with clinical presentation (Table 25-1, Figs. 25-3 and 25-4).

**B. Vascular Rings**

1. **Vascular rings and other masses** that extrinsically obstruct the lower airways can be imaged with contrast-enhanced CT or MRI.
2. **Tracheomalacia and intrinsic masses** can be studied with bronchoscopy.

**C. Foreign Bodies**

1. **Lower airway foreign bodies:** In the absence of a radiopaque foreign body, radiologic findings include air trapping, hyperinflation, atelectasis, consolidation, pneumothorax, and pneumomediastinum. Further studies should include expiratory films (in a cooperative patient), bilateral decubitus chest films (in an uncooperative patient), or airway fluoroscopy.
2. **Esophageal foreign bodies:** Usually lodged at one of three locations—thoracic inlet, level of aortic arch and left mainstem bronchus, or gastroesophageal junction. Evaluation should include:
  - a. Lateral airway film (include nasopharynx)
  - b. AP film of chest and abdomen (including supraclavicular region)
  - c. Contrast study of esophagus if other films are normal. If perforation is suspected, use nonionic water-soluble contrast.

**TABLE 25-1**

**DIAGNOSIS OF DISEASES BASED ON AIRWAY RADIOLOGIC EXAMINATION**

Diagnosis	Findings on Airway Films
Croup	AP and lateral films with subglottic narrowing ( <i>steeple sign</i> )
Epiglottitis	Enlarged, indistinct epiglottis on lateral film ( <i>thumbprint sign</i> )
Vascular ring	AP and lateral films with narrowing; double or right aortic arch
Retropharyngeal abscess or pharyngeal mass	Soft tissue air or persistent enlargement of prevertebral soft tissues; more than half of a vertebral body above C3 and one vertebral body below C3
Immunodeficiency	Absence of adenoidal and tonsillar tissue after age 6 mo

AP, Anteroposterior.

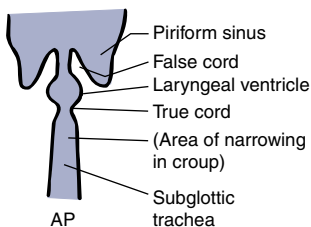


FIGURE 25-3

Anteroposterior (AP) neck film with normal anatomy on AP airway view.

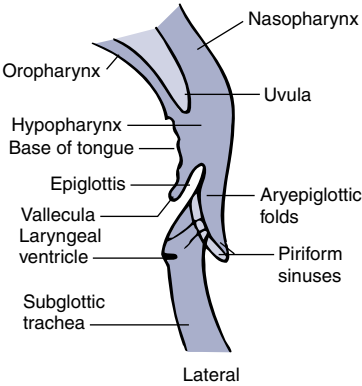
## VI. CHEST <sup>34</sup>

### A. Posteroanterior and Lateral Radiographs

First images obtained when studying the chest (Figs. 25-5 and 25-6).

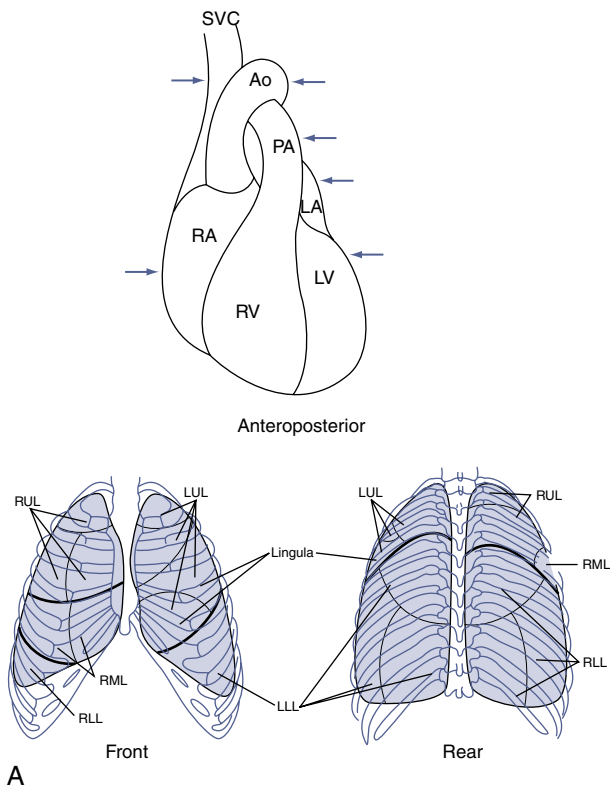
### B. Pneumonia

1. **Lobar or segmental consolidation:** More typical of bacterial infections
2. **Hyperinflation, bilateral patchy or streaky densities, and peribronchial thickening:** More typical of nonbacterial disease



**FIGURE 25-4**

Lateral neck film with normal anatomy on lateral airway view.

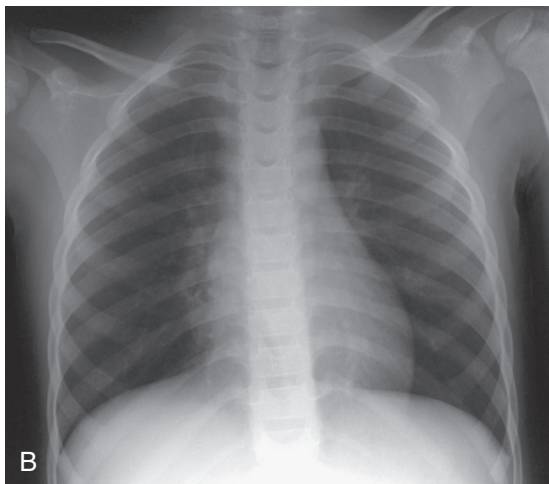
**FIGURE 25-5**

**A**, Normal lung and cardiac anatomy as seen on an anteroposterior chest radiograph. Arrows indicate contours seen on anteroposterior chest x-ray films (**B**). Ao, Aorta; LA, left atrium; LLL, left lower lobe; LUL, left upper lobe; LV, left ventricle; PA, pulmonary artery; RA, right atrium; RLL, right lower lobe; RML, right middle lobe; RUL, right upper lobe; RV, right ventricle; SVC, superior vena cava. (Heart diagram modified from Kirks DR, Griscom NT. *Practical Pediatric Imaging: Diagnostic Radiology of Infants and Children*. 3rd ed. Philadelphia: Lippincott-Raven, 1998.)

*Continued*

### C. Atelectasis vs. Infiltrate

1. **Atelectasis:** When air is removed from the lung, tissue collapses, resulting in volume loss on chest radiographs. If severe enough, mediastinum and/or diaphragm are pulled toward the lesion. Air may still remain in

**FIGURE 25-5, cont'd**

larger bronchi, creating air bronchograms on radiograph. Collapse and reexpansion can occur quickly.

2. **Infiltrate:** Fluid (blood, pus, edema) that invades one of the compartments of the lung (bronchoalveolar air space or peribronchial interstitial space), seen as a density on radiograph. When alveolar air is displaced by fluid but air remains in bronchi, classic pneumonic infiltrate with air bronchograms is seen. When infiltrate is interstitial, its borders can be vague and bronchial walls may be thickened. Typically, infiltrates resolve in 2–6 weeks.

#### **D. Parapneumonic Effusions and Empyema**

Initially, PA and lateral radiographs are obtained. Lateral decubitus radiographs may also be helpful. Ultrasound is often the best modality for early identification of loculation, but a contrast-enhanced CT may be necessary to further delineate loculation or differentiate between pleural fluid and collapsed or consolidated tissue.

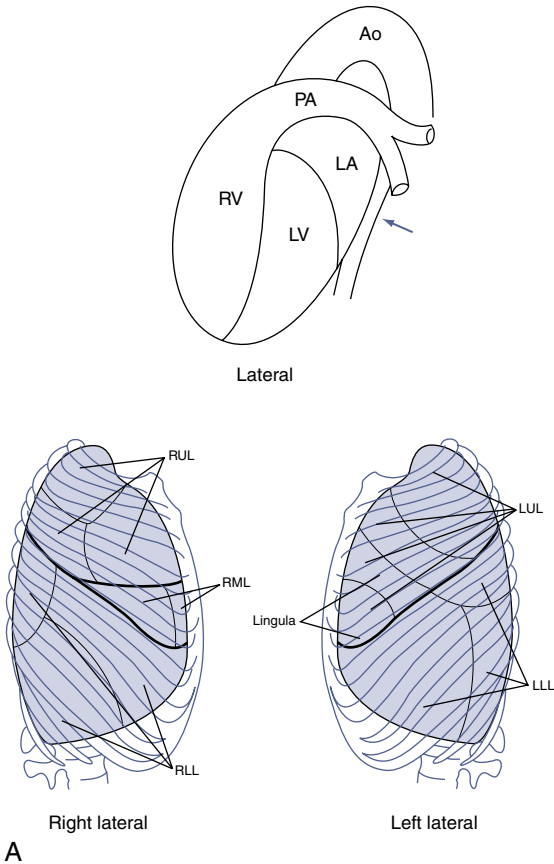
#### **E. Parenchymal Findings**

1. **Lung abscess, cavitory necrosis, lung contusions:** Best imaged with contrast-enhanced CT.
2. **Pneumatocele, fungal infections, interstitial lung disease:** Use non-contrast CT.

#### **F. Mediastinal Masses**

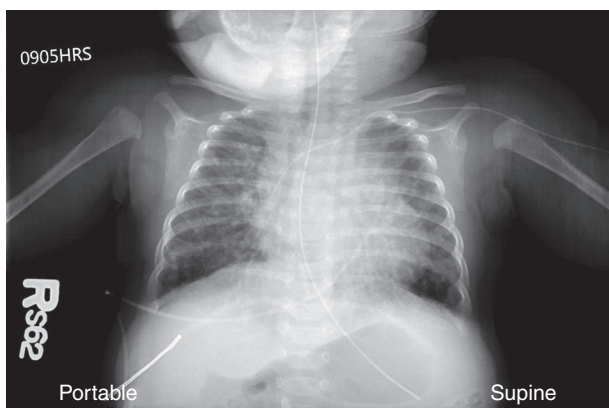
Mediastinal masses (thymus, lymphoma, bronchogenic cyst, neuroblastoma, neurofibroma) are initially imaged with plain films, followed by contrast-enhanced CT or MRI.



**FIGURE 25-6**

**A**, Normal lung and cardiac anatomy as seen on lateral chest radiograph. Arrow indicates contours seen on lateral chest x-ray films (**B**). Ao, Aorta; LA, left atrium; LLL, left lower lobe; LUL, left upper lobe; LV, left ventricle; PA, pulmonary artery; RLL, right lower lobe; RML, right middle lobe; RUL, right upper lobe; RV, right ventricle. (*Heart diagram modified from Kirks DR, Griscom NT. Practical Pediatric Imaging: Diagnostic Radiology of Infants and Children. 3rd ed. Philadelphia: Lippincott-Raven, 1998.*)

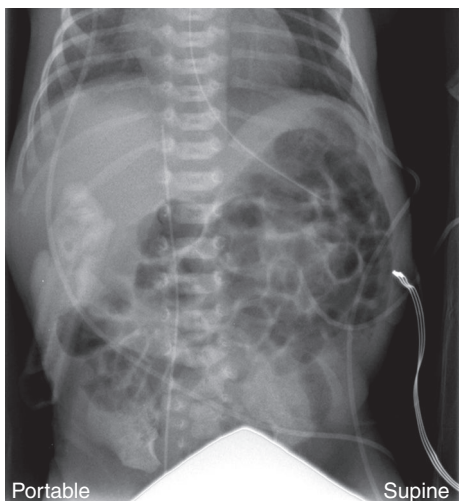
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**FIGURE 25-6, cont'd****FIGURE 25-7**

Central line placement on anteroposterior chest radiograph for line inserted in arm or neck.

### G. Central Line Placement

On chest radiograph, central venous catheters entering from the neck or arm are ideally placed with catheter tip at junction of superior vena cava and right atrium. Some extension into right atrium is acceptable, but if catheter is noted to curve to patient's left on PA film, catheter may be positioned in right ventricle (Fig. 25-7). Catheters inserted below diaphragm should be placed with tip at level of diaphragm (Fig. 25-8).

**FIGURE 25-8**

Central line placement on anteroposterior radiograph for line inserted below the diaphragm.

### H. Endotracheal Tube (ETT) Placement

On chest radiograph, end of the ETT should rest about midway between thoracic inlet and carina. Lung fields should show symmetric aeration.

## VII. HEART AND VESSELS 3

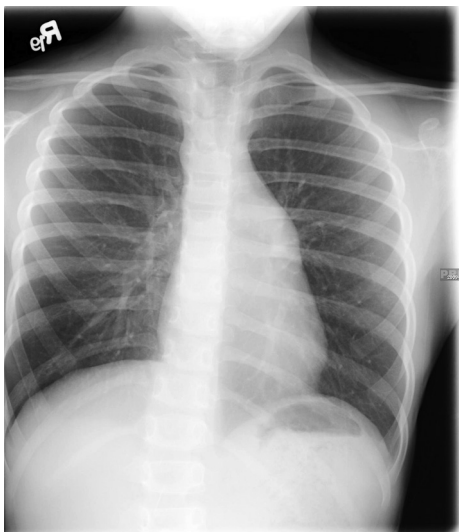
### A. Congenital Heart Disease

Most clearly defined by echocardiography, but initial PA and lateral chest radiograph may yield important clues:

1. **Position of aortic arch:** Left or right (Fig. 25-9)
2. **Situs:** Noting position of apex, stomach bubble, and liver
3. **Heart size:** With particular attention paid to lateral chest radiograph
4. **Pulmonary vascularity:** Increased or decreased flow in arteries and veins

### B. Vessels

1. **Moving blood is detected by ultrasonographic frequency shifts.**
2. **Color Doppler flow imaging:** Can be used to evaluate deep vein thrombosis (DVT), vascular patency, intracranial blood flow (including transcranial Doppler [TCD] to screen for ischemic brain injury risk in sickle cell disease), cardiac shunt flow, transplant vascularity, veno-occlusive disease of the liver, and testicular perfusion in testicular torsion.
3. **Power Doppler** is particularly sensitive in detecting slow flow in small vessels (e.g., infant testes).

**FIGURE 25-9**

Right aortic arch as seen on anteroposterior chest radiograph.

### C. Vessel Abnormalities

Can be studied with echocardiography/US, CT, and MRI. Use these modalities to detect coarctation of the aorta, aortic stenosis, pulmonary artery and vein abnormalities, vascular rings, arteriovenous malformations (AVMs), hemangiomas, aneurysms, and postoperative complications like thrombosis and stenosis.

## VIII. ABDOMEN

### A. Neonatal Enterocolitis

Clinically diagnosed and followed by abdominal radiographs, which may show focal dilation, featureless loops, pneumatosis, and portal venous gas.

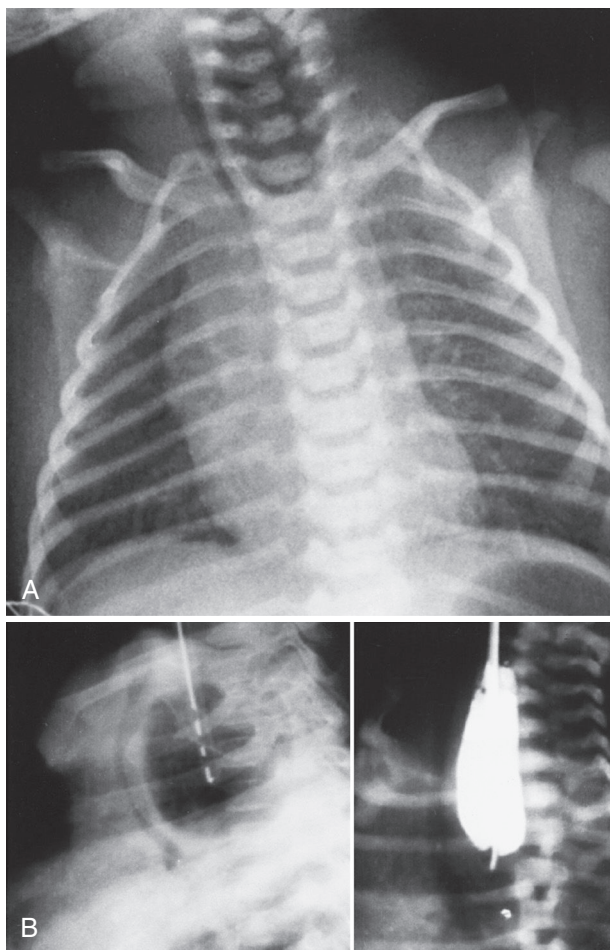
### B. Esophageal Atresia and Tracheoesophageal Fistula (Fig. 25-10)

Studied initially with chest radiographs, which may reveal the air-distended esophageal atretic pouch, nasogastric tube curled up in this pouch, or excessive dilation of stomach as a result of fistula communication.

### C. High Intestinal Obstruction

1. **Diagnosed with upper gastrointestinal (UGI) series:** Contrast is ingested, and esophagus, stomach, and duodenum are visualized.

Causes: Esophageal webs and rings, masses, duodenal atresia or webs (Fig. 25-11), annular pancreas, midgut volvulus, and Ladd bands.

**FIGURE 25-10**

Esophageal atresia and tracheoesophageal fistula. **A**, Frontal chest examination reveals lucency over cervical and upper thoracic spine (blind-ending esophageal pouch filled with air) and air within stomach, typical for esophageal atresia with tracheoesophageal fistula. **B**, Tube has been placed in blind-ending pouch, and contrast material injected on subsequent film. Airway is bowed forward and in varying degrees of collapse on these two images. (From Slovis TL. Caffey's Pediatric Diagnostic Imaging. 11th ed. Philadelphia: Mosby, 2008.)

**FIGURE 25-11**

Newborn with duodenal atresia. Portable abdominal radiograph shows dilated stomach and proximal duodenum ("double-bubble" sign), with absent distal gas. (From Slovis TL. *Caffey's Pediatric Diagnostic Imaging*. 11th ed. Philadelphia: Mosby, 2008.)

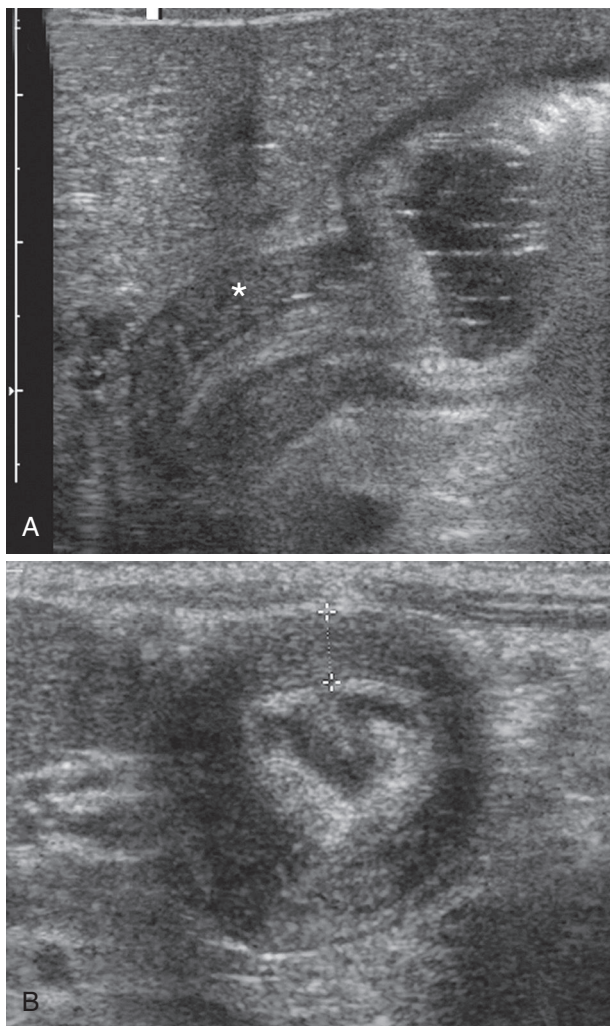
2. **UGI** can also help evaluate hiatal hernias, varices, gastric outlet obstruction, motility problems, ulcerations, and reflux.
3. **During UGI**, identifying duodenojejunal junction (ligament of Treitz) helps diagnose malrotation. Normally the junction is to the left of spine, at or above level of duodenal bulb.

#### **D. Pyloric Stenosis**

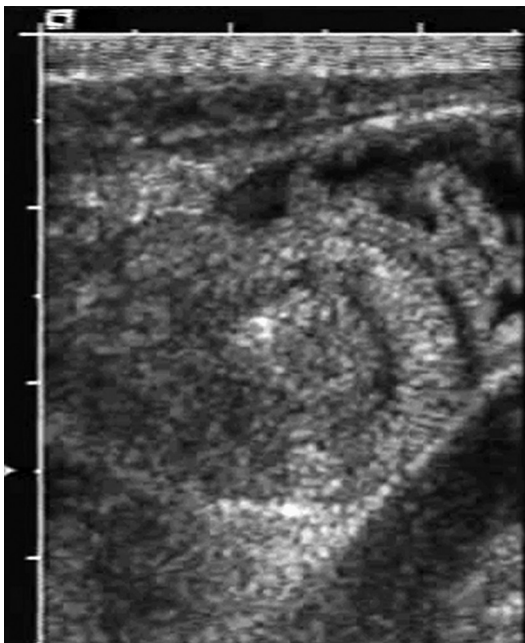
1. **US is the preferred examination** because it directly visualizes the pyloric muscle. Normal pylorus is <17 mm in length, and its muscular wall is <4 mm in width (Fig. 25-12).
2. **Radiographs:** Show gastric distention.
3. **UGI:** Delayed gastric emptying and a narrow pyloric channel will be evident.

#### **E. Bowel Obstruction**

1. **Determination of large or small bowel obstruction:** Often aided by supine radiograph, prone radiograph, and either upright, supine cross-table lateral, or left lateral decubitus film to look for free air and air-fluid levels. Causes of obstruction: Adhesions, appendicitis, incarcerated inguinal hernias, Meckel diverticulum, intussusception.
2. **US can be helpful** in thin patients and female patients who have ovarian pathology in their differential for abdominal pain.
3. **CT with intravenous, oral, or rectal contrast is more useful** with an obese patient or when looking for perforated appendicitis or abscess.

**FIGURE 25-12**

Abdominal ultrasound for diagnosis of hypertrophic pyloric stenosis. **A**, Ten minutes after dextrose solution was given, pyloric muscle (*asterisk*) was better seen, and canal length was easier to evaluate. **B**, “Doughnut” sign of hypertrophic pyloric stenosis in infant imaged in **A**. Fixed circumferential thickening of pylorus may resemble a doughnut in image taken perpendicular to long axis of stomach. Calipers mark the anterior muscle, which measures more than 3 mm. Thickened mucosa is seen centrally. Note that echogenicity of the muscle perpendicular to ultrasound beam in near field and far field is greater than that seen in lateral aspects of thickened pyloric muscle. (From Slovis TL. Caffey’s Pediatric Diagnostic Imaging. 11th ed. Philadelphia: Mosby, 2008.)



**FIGURE 25-13**

Abdominal ultrasound shows short segment intussusception. Longitudinal ultrasound image along right flank of an infant with proven viral gastroenteritis shows short-segment intussusception that occurred during the examination. Visible peristaltic activity of the intussusceptum within the intussuscipiens was visible in real time. Intussusception resolved spontaneously. (From Slovis TL. Caffey's Pediatric Diagnostic Imaging. 11th ed. Philadelphia: Mosby, 2008.)

4. **Contrast enemas with dilute water-soluble agents** can also be useful in lower intestinal obstruction in the newborn.

#### **F. Intussusception**

1. **On abdominal radiographs**, particularly prone view, findings include minimal gas in right abdomen and ascending colon.
2. **US will show alternating rings.** Doppler will show flow in the intussuscepted mesentery, which will allow confirmation of the diagnosis as well as assessment of viability of the intussusceptum (Fig. 25-13).
3. **For fluoroscopy-guided therapeutic enema**, air insufflation is preferred, but other contrast agents may also be used. Reducing an intussusception with air or contrast is contraindicated if perforation is suspected.

#### **G. Meckel Diverticulum**

Suggested by painless lower GI bleeding; diagnosed by nuclear scintigraphy using technetium-99m ( $^{99m}\text{Tc}$ )-pertechnetate.



## H. Abdominal Trauma

CT of abdomen and pelvis to detect solid organ injury, vascular extravasation, free fluid, bowel wall thickening, and organ laceration.

## I. Biliary Atresia

1. **In neonates with jaundice**, US initially to distinguish biliary atresia from hepatitis. Gallbladder will be small or absent with biliary atresia.
2. **Hepatobiliary scintigraphy with  $^{99m}\text{Tc}$ -iminodiacetate (HIDA) reveals** absence of radionuclide in GI tract, with biliary atresia.

## J. Nasoduodenal (ND) Tube Placement

Visualize tube on a plain abdominal AP film passing through stomach, crossing midline, and passing into duodenal bulb (where tip of tube will just begin to point inferiorly). If it remains unclear whether tube is in duodenum or coiled in stomach, a lateral film is indicated (a properly placed ND tube tip will lie posterior, near the spine).

## IX. GENITOURINARY TRACT 3

### A. Urinary Tract Infection (UTI)

1. **Initial febrile UTIs in children <5 years** require imaging to look for congenital anomalies (e.g., posterior urethral valves, ureterocele), vesicoureteral reflux, baseline renal measurements, and damage to kidney cortices.
2. **Workup first includes US to diagnose** hydronephrosis, ureteropelvic junction obstruction, posterior urethral valves, multicystic dysplastic kidneys, chronic pyelonephritis, renal fusion (horseshoe kidney), and renal cysts.
3. **If clinically indicated**, voiding cystourethrogram (VCUG) can be performed to diagnose vesicoureteral reflux, abnormalities of bladder or urethral function and anatomy (including ureterocele), and posterior urethral valves.
4. **Occasionally, dimercaptosuccinic acid (DMSA) scan** is useful in following renal cortical scarring and pyelonephritis.

### B. Uterine and Ovarian Pathology

Transvaginal or transabdominal US should be performed if the clinical picture is suspicious for ovarian torsion, tubo-ovarian abscess (TOA), or ectopic pregnancy.

## X. EXTREMITIES 3.5

### A. Trauma

1. **Adequate evaluation requires AP and lateral radiographs.** Restricting the film to include only the area of interest improves resolution (e.g., for a thumb injury, ask for an image of the thumb, not the hand).
2. **Comparison films of the uninvolved extremity are not necessary but may be helpful**, such as in evaluation of joint effusions (particularly hip), suspected osteomyelitis, or pyarthrosis and/or evaluation of subtle fractures, especially in areas of multiple ossification centers such as the elbow.

3. **Salter-Harris classification of growth-plate injury** (Table 25-2).
4. **Avulsion injuries** tend to occur at the knee and pelvis.

#### B. Stress Fractures

1. **Occur most often at the tibia, fibula, metatarsals, and calcaneus.**
2. **Radiography will show a band of sclerosis and new bone formation.**
3. **Skeletal scintigraphy is a sensitive method for making the diagnosis.**

#### C. Osteomyelitis

1. **Tends to occur at metaphysis of long bones and within flat bones.**
2. **Radiography will show deep soft-tissue swelling and bony changes** (may take 10 days to appear).
3. **Skeletal scintigraphy and MRI** will often be positive before radiographic changes are noticeable.

#### D. Hip Disorders



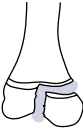

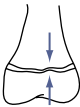
1. **Developmental hip dysplasia** (congenital hip dislocation) is imaged initially with US. Once femoral heads ossify, radiographs are more helpful (Fig. 25-14).
2. **Legg-Calvé-Perthes disease** (avascular necrosis of femoral head) can be imaged with AP and frog-leg lateral hip films as well as MRI and bone scintigraphy (Fig. 25-15).
3. **Slipped capital femoral epiphysis** (SCFE) will show femoral head displacement on frog-leg lateral and AP radiographs (Fig. 25-16).

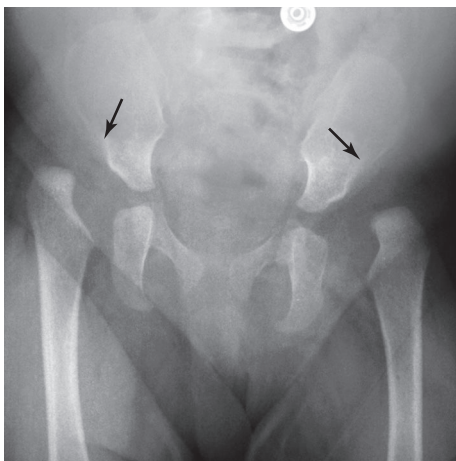
#### E. Bone Lesions

1. **Osteochondroma:** Benign lesion that arises from the metaphysis of a long bone, most frequently the distal femur, proximal humerus, and proximal tibia. Composed of cortical and medullary bone with a cap of hyaline cartilage and is continuous with the cortex and intramedullary cavity of the involved bone (Fig. 25-17).
2. **Unicameral bone cyst:** Benign lesion that appears on radiographs as a solitary, centrally located, lucent lesion located within the medullary portion of the bone and often extends to the physis. Tend to occur in the proximal femur or humerus (Fig. 25-18).
3. **Fibroma:** Benign lesion that appears on radiographs as a lucency in the metaphyseal cortex, highlighted by a sclerotic, often scalloped border (Fig. 25-19).
4. **Osteoma:** Benign lesion that appears on radiographs as a small, oval lucency in the metaphysis or diaphysis. Most frequently occurs in the proximal femur and tibia, although any bone can be involved, including vertebrae. Often present with gradually increasing pain that is worse at night (Fig. 25-20).
5. **Osteosarcoma:** Most common primary malignant bone tumor in children and adolescents >10 years of age. Lesion typically occurs at the metaphyses of long bones, and radiographs demonstrate sclerotic deconstruction, although sometimes lytic, with a classic sunburst pattern (Fig. 25-21).

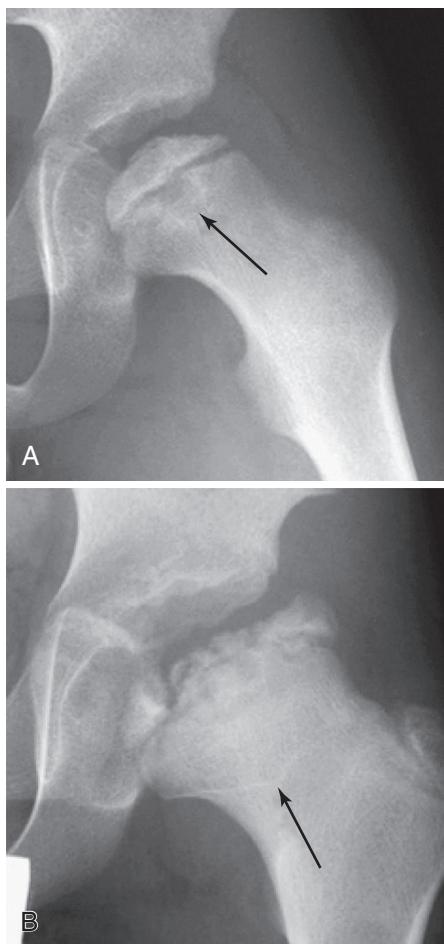
TABLE 25-2

**SALTER-HARRIS CLASSIFICATION OF GROWTH PLATE INJURY**

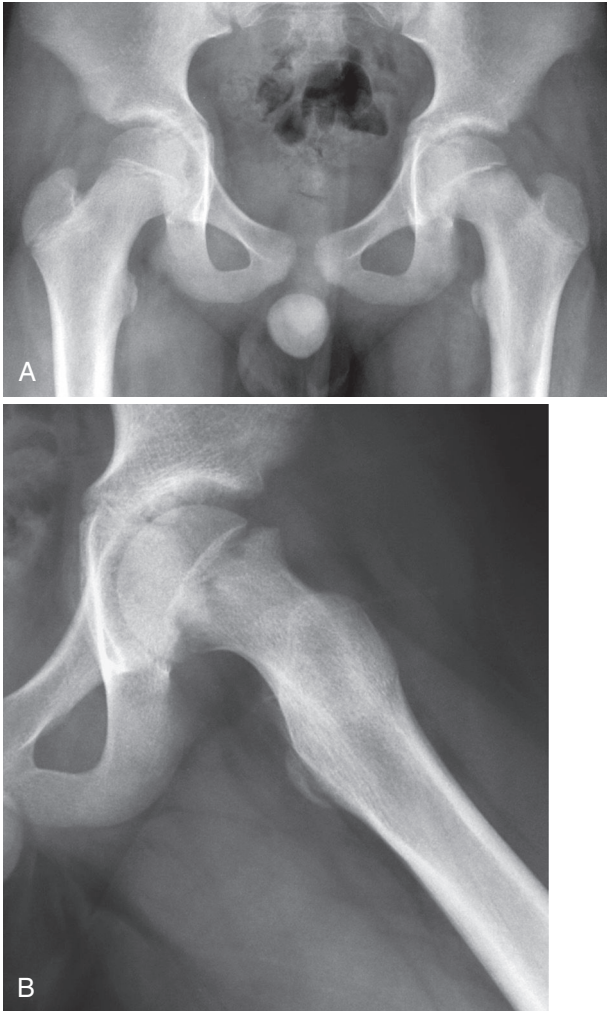
Class I	Class II	Class III	Class IV	Class V
Fracture along growth plate	Fracture along growth plate with metaphyseal extension	Fracture along growth plate with epiphyseal extension	Fracture across growth plate, including metaphysis and epiphysis	Crush injury to growth plate without obvious fracture
I	II	III	IV	V
				

**FIGURE 25-14**

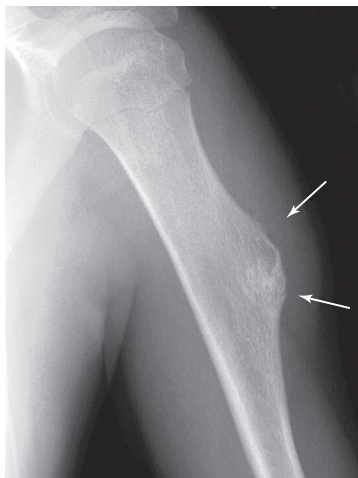
Neutral anteroposterior (AP) view of a 3-month-old girl shows bilateral shallow acetabula, dislocated hips, and early pseudoacetabulum formation (arrows). (From Slovis TL. Caffey's Pediatric Diagnostic Imaging. 11th ed. Philadelphia: Mosby, 2008.)

**FIGURE 25-15**

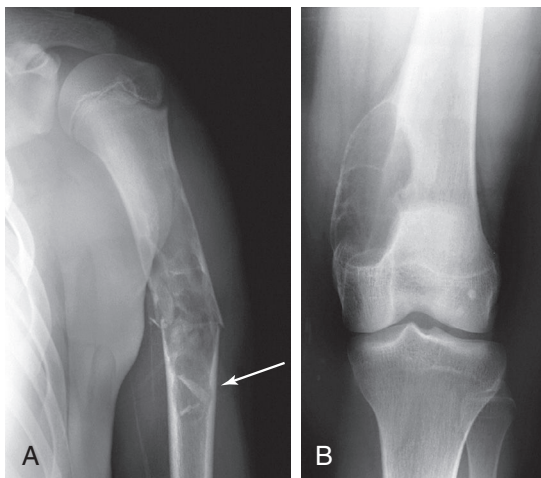
A 7-year-old boy with a limp and osteonecrosis of left proximal femoral epiphysis. **A**, Radiograph of left hip reveals a small, sclerotic proximal femoral epiphysis with an irregular joint surface. Metaphysis of proximal femur also shows cystic changes (*arrow*) that indicate a poor prognosis. **B**, At 18 months after presentation, radiograph of left hip reveals further fragmentation and continued lateral extrusion of epiphysis. Acetabulum is beginning to impinge on uncovered portion of lateral column, and incongruence of hip joint is apparent. The "sagging rope" sign (*arrow*), produced by the outline of an abnormally oriented physis, indicates growth arrest. Widening of femoral neck is seen ("coxa magna"). (From Slovis TL. Caffey's Pediatric Diagnostic Imaging. 11th ed. Philadelphia: Mosby, 2008.)

**FIGURE 25-16**

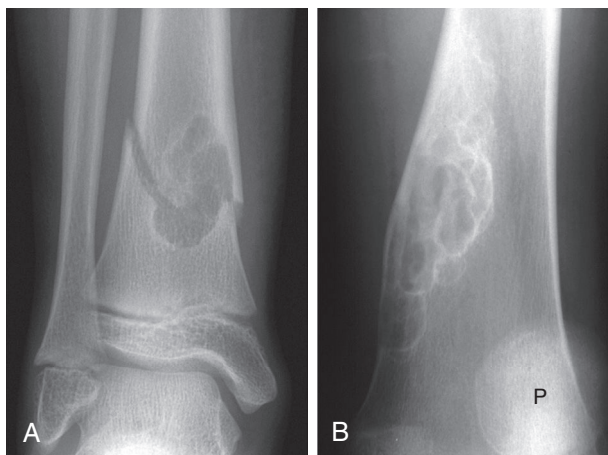
Slipped capital femoral epiphysis in 11-year-old boy with left hip pain. **A**, On anteroposterior view, growth plate of left proximal femur is wide and indistinct. No portion of left femoral head projects lateral to Klein line. Right proximal femur is normal. **B**, On lateral view, malalignment of femoral head and neck at growth plate is better seen. Femoral head is displaced posteromedially relative to femoral neck but is still in continuity. (From Slovis TL. Caffey's Pediatric Diagnostic Imaging. 11th ed. Philadelphia: Mosby, 2008.)

**FIGURE 25-17**

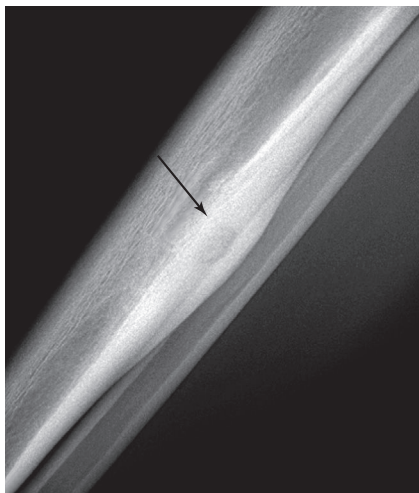
Sessile osteochondroma (arrows) of proximal humeral diaphysis in a 16-year-old girl. (From Slovis TL. Caffey's Pediatric Diagnostic Imaging. 11th ed. Philadelphia: Mosby, 2008.)

**FIGURE 25-18**

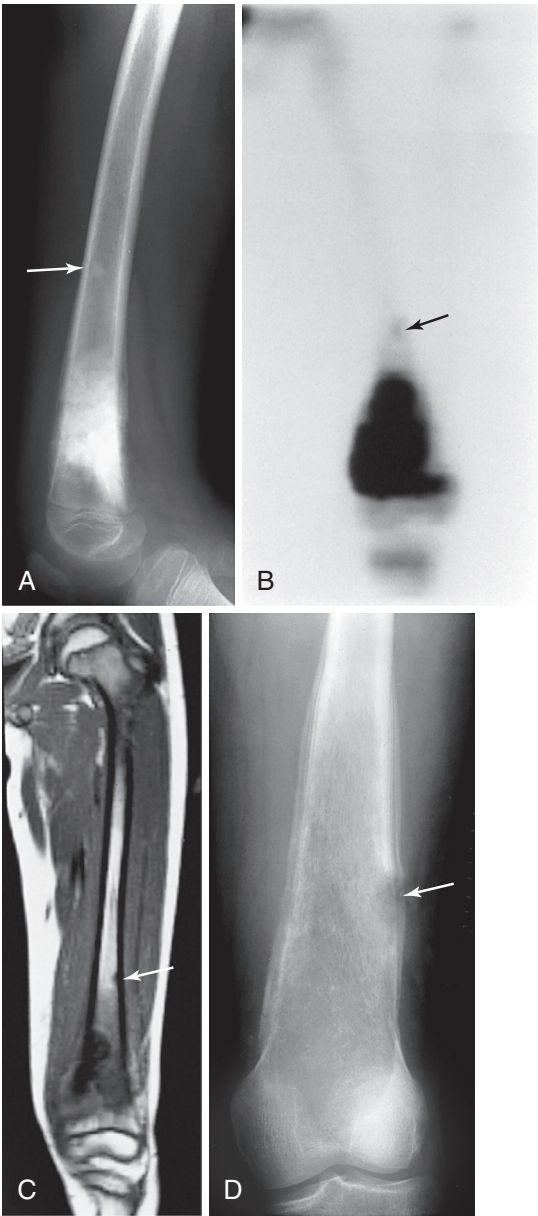
**A**, Simple bone cyst with pathologic fracture in a 12-year-old boy. Cyst has thinned and scalloped overlying cortex. A fallen fragment is noted (arrow). **B**, Aneurysmal bone cyst in a 13-year-old. Radiograph of knee shows an eccentric, expansile lucent lesion with a thin, bony shell involving medial aspect of distal femur. (From Slovis TL. Caffey's Pediatric Diagnostic Imaging. 11th ed. Philadelphia: Mosby, 2008.)

**FIGURE 25-19**

**A**, Pathologic fracture through a nonossifying fibroma in a 10-year-old boy. Lesion has well-defined, minimally sclerotic margins. **B**, Large, lobulated nonossifying fibroma in a 16-year-old boy; anteroposterior view of distal femur. Proximal portion of lesion is sclerotic, consistent with early involution. P, Patella. (From Slovis TL. Caffey's Pediatric Diagnostic Imaging. 11th ed. Philadelphia: Mosby, 2008.)

**FIGURE 25-20**

Osteoid osteoma of tibia in a 15-year-old girl. Radiograph shows cortical thickening posteriorly. Lucent nidus is faintly seen (arrow). (From Slovis TL. Caffey's Pediatric Diagnostic Imaging. 11th ed. Philadelphia: Mosby, 2008.)





**FIGURE 25-21**

**A**, Lateral radiograph of femur of a 9-year-old boy with osteosarcoma shows a sclerotic intramedullary distal femoral tumor with slight periosteal new bone formation. A small, dense skip metastasis (*arrow*) is seen proximal to primary tumor of main tumor mass. Skip metastasis (*arrow*) is also seen on a technetium-99m methylene diphosphonate bone scan (**B**) and is shown as a cortical-based intramedullary lesion (*arrow*) on a coronal T1-weighted magnetic resonance image (**C**). **D**, Radiograph of femur of a 16-year-old boy with telangiectatic osteosarcoma shows large lesion in distal meta-diaphysis extending into epiphysis. Tumor is lytic rather than bone forming. There is mild periosteal reaction. There has been a recent incisional biopsy (*arrow*). (From Slovis TL. Caffey's Pediatric Diagnostic Imaging. 11th ed. Philadelphia: Mosby, 2008.)

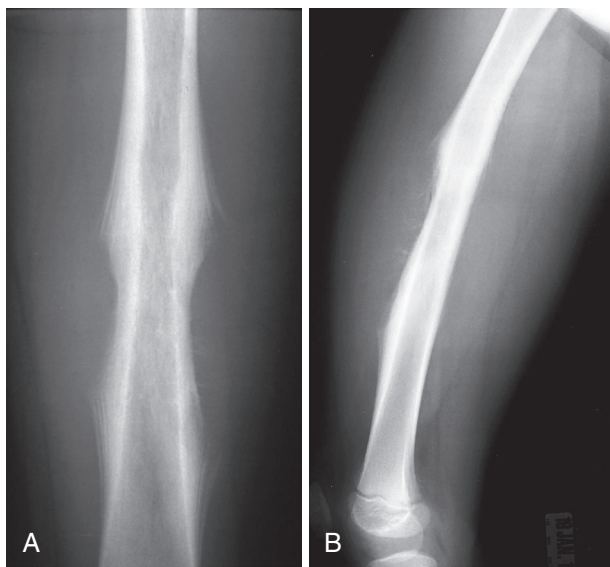
6. **Ewing sarcoma:** Second most common primary malignant bone tumor in children and adolescents >10 years of age; most common primary malignant bone tumor in children <age 10. Lesion is typically in the diaphyses of long and flat bones, and radiographs demonstrate a lytic lesion with periosteal reaction, creating a classic lamellar "onion-skinning" appearance. CT or MRI of lesion may demonstrate a soft-tissue mass (Fig. 25-22).

#### F. Bone Age

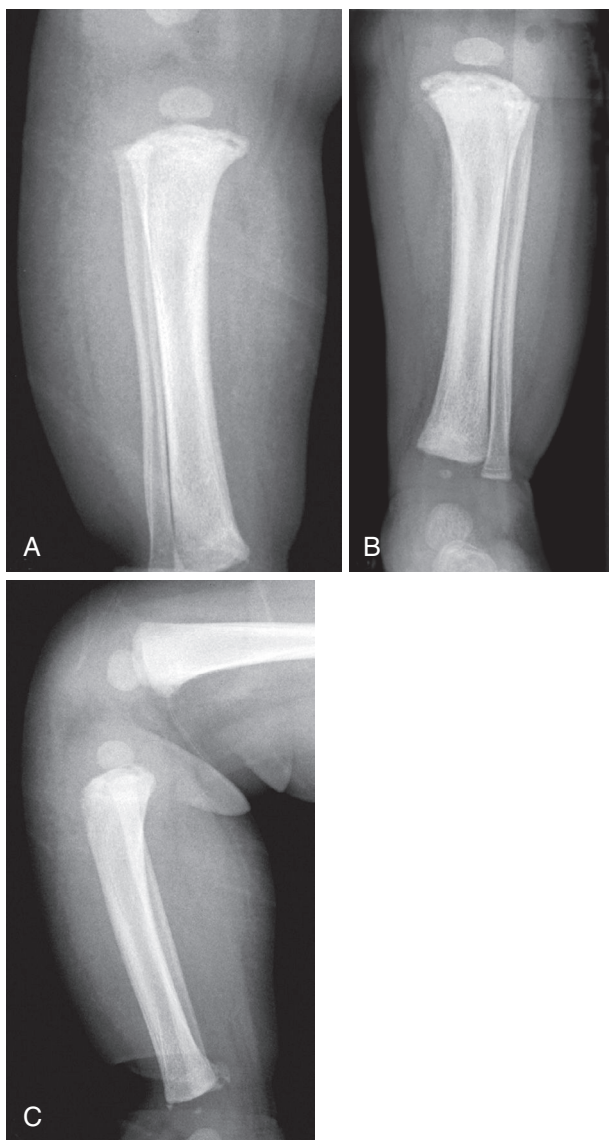
Obtain a PA view of the left hand and wrist.

#### G. Skeletal Survey

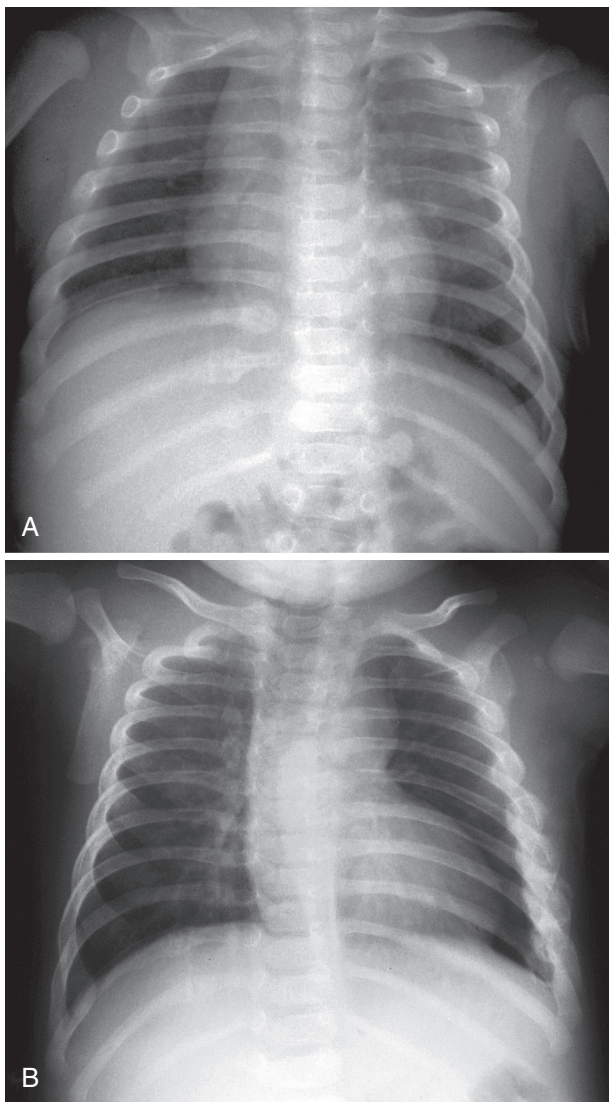
1. **In cases of suspected child abuse,** should include lateral skull film with C-spine film, AP chest film (bone technique), oblique views of ribs, AP view of pelvis, abdominal film (bone technique) with lateral thoracic and lumbar spine, and AP long-bone films.
2. **Classic findings:** Multiple metaphyseal injuries (especially corner and bucket-handle fractures) and other fractures of various ages (Fig. 25-23). Suspicion should also be raised by fracture at unusual sites, such as posterior rib fractures or solitary spiral and transverse long-bone fractures with an inconsistent history of trauma (Fig. 25-24).

**FIGURE 25-22**

Anteroposterior (**A**) and lateral (**B**) radiographs of femur of a 6-year-old girl show a Ewing sarcoma arising from mid-diaphysis. Lamellar periosteal reaction and new bone formation are present, with Codman triangles at proximal and distal ends of tumor. Faint periosteal new bone extends perpendicularly into soft-tissue component of tumor. Medulla is not expanded. (From Slovis TL. Caffey's Pediatric Diagnostic Imaging. 11th ed. Philadelphia: Mosby, 2008.)

**FIGURE 25-23**

Anteroposterior right (A) and left (B) lower leg and lateral right (C) lower leg of 3-month-old male infant transferred with acute occipital skull fracture, classic metaphyseal lesions of distal femora and proximal and distal tibiae, and 23 rib fractures. (From Slovis TL. Caffey's Pediatric Diagnostic Imaging. 11th ed. Philadelphia: Mosby, 2008.)

**FIGURE 25-24**

A 6-week-old male infant sent for an upper gastrointestinal series for evaluation of colicky pain was found to have healing rib fractures. **A**, Initial chest x-ray identifies healing fractures at the right 9th, 10th, and 11th ribs. **B**, Follow-up chest film 2 weeks later shows additional fractures, now healing, at lateral aspect of left 3rd through 9th ribs. Father admitted to shaking the infant. (From Slovis TL. Caffey's Pediatric Diagnostic Imaging. 11th ed. Philadelphia: Mosby, 2008.)

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1. Frush DP, Donnelly LF, Rosen NS. Computed tomography and radiation risks: what pediatric health care providers should know. *Pediatrics*. 2003;112:951-957.
2. Kirks DR, Griscom NT. *Practical Pediatric Imaging: Diagnostic Radiology of Infants and Children*. 3rd ed. Philadelphia: Lippincott-Raven, 1998.
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# Chapter 26

## Rheumatology

Steven C. Marek, MD

 See additional content on Expert Consult

### I. WEBSITE

American College of Rheumatology: <http://www.rheumatology.org/>

### II. LABORATORY STUDIES

Most laboratory studies used to diagnose rheumatic diseases are nonspecific, and results must be interpreted within the context of the full clinical picture. Once a diagnosis is established, however, they can be used to follow the condition's clinical course, indicating flares or remission of the rheumatic disease. Sensitivities and specificities of rheumatologic tests must be considered with any clinical decision (see Chapter 28).

#### A. Acute-Phase Reactants

##### 1. Overview:

- Indicate presence of inflammation when elevated.
- Elevation is nonspecific and can result from trauma, infection, rheumatic diseases, or malignancy.<sup>1</sup>
- Markers include erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), platelet count, ferritin, haptoglobin, fibrinogen, serum amyloid A, and complement.<sup>1,2</sup>

##### 2. ESR:

- Measure of the rate of fall of red blood cells in anticoagulated blood within a vertical tube; reflects level of rouleaux formation caused by acute phase reactants.<sup>1</sup>
- Can be falsely lowered in afibrinogenemia, anemia, and sickle cell disease; these states interfere with rouleaux formation.<sup>2</sup>
- Levels vary depending on age, ethnicity, gender, and freshness of blood sample.<sup>1</sup>
- Serial measurements may help in monitoring disease severity/activity in conditions such as systemic lupus erythematosus (SLE) and juvenile idiopathic arthritis (JIA).

##### 3. CRP<sup>1,3,4</sup>:

- Synthesized by the liver; assists in clearance of pathologic bacteria and damaged cells via activation of complement-mediated phagocytosis; mediates acute inflammation by altering cytokine release and is thought to prevent autoimmunity by binding to and masking autoantigens.
- Increases and decreases rapidly owing to short half-life ( $\approx 18$  hours).
- Elevation is nonspecific, indicating only inflammation:
  - (1) Most active phases of rheumatic disease result in elevation to 1–10 mg/dL.

- (2) Level >10 mg/dL raises concern for bacterial infection or systemic vasculitis.

## B. Autoantibodies (Table 26-1)

The positive predictive value of any autoantibody assay depends on clinical context. These studies can prove valuable in confirming clinical suspicion. However, in the absence of suspicion, they have low yield and may be misleading.

### 1. Antinuclear antibody (ANA):

- Nonspecific test for rheumatic disease.<sup>1</sup>
- Positive in ≈60%–70% of children with an autoimmune disease, but can be seen in ≈15%–35% of normal persons.
- If positive, consider ordering individual autoantibodies (see Table 26-1).
- Can be positive in nonrheumatic diseases:
  - Neoplasm
  - Infections (transiently positive): Mononucleosis, endocarditis, hepatitis, malaria
- If positive in pauciarticular JIA, there is increased risk of uveitis.

### 2. Rheumatoid factor (RF)<sup>1</sup>:

- Immunoglobulin (Ig)M antibodies to the Fc portion of IgG
- Positive in rheumatic and nonrheumatic disease:
  - Rheumatic diseases: SLE, mixed cryoglobulinemia, JIA (rarely), mixed connective tissue disease, and Henoch-Schönlein purpura
  - Infections: Hepatitis B, bacterial endocarditis, tuberculosis, and toxoplasmosis, other, rubella, cytomegalovirus, and herpes (TORCH) infections

TABLE 26-1

## AUTOANTIBODIES ASSOCIATED WITH COMMON RHEUMATOLOGIC DISEASES

Systemic Lupus Erythematosus (SLE)	Juvenile Idiopathic Arthritis*	Vasculitis	Polymyositis/Dermatomyositis
<ul style="list-style-type: none"> <li>Antinuclear antibody (ANA)</li> <li>Anti-double stranded DNA</li> <li>Anti-Smith</li> <li>Antiribonucleoprotein (anti-RNP)</li> <li>Antimicrosomal</li> <li>Antiphospholipids†</li> </ul>	<ul style="list-style-type: none"> <li>Rheumatoid factor (RF)</li> <li>Anti-cyclic citrullinated peptide (anti-CCP)</li> <li>ANA</li> </ul>	<ul style="list-style-type: none"> <li>Antineutrophil cytoplasmic antibody (ANCA)—cytoplasmic/proteinase-3 (PR3)</li> <li>ANCA—perinuclear/MPO (myeloperoxidase)</li> </ul>	<ul style="list-style-type: none"> <li>ANA</li> <li>Anti-Jo-1</li> </ul>
Mixed Connective Tissue Disease	Drug-Induced SLE	Sjögren Syndrome	Scleroderma
<ul style="list-style-type: none"> <li>ANA</li> <li>Anti-RNP</li> </ul>	<ul style="list-style-type: none"> <li>Antihistone</li> </ul>	<ul style="list-style-type: none"> <li>ANA</li> <li>Anti-Ro</li> <li>Anti-La</li> </ul>	<ul style="list-style-type: none"> <li>ANA</li> <li>Anticentromere</li> <li>Anti-RNP</li> <li>Antitopoisomerase (anti-Scl-70)</li> </ul>

\*JIA is typically RF and CCP negative; when positive may indicate erosive disease.

†Antiphospholipids: anticardiolipin, lupus anticoagulant, and antiglycoprotein I.

Modified from Kliegman RM, Behrman RE, Jenson HB, et al. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia: Saunders Elsevier, 2007.

- c. Negative RF: Does not rule out rheumatic disease
- d. Prognostic importance in polyarticular JIA: Positive RF suggests more progressive disease (see Section III)

**3. Anti-cyclic citrullinated peptide (anti-CCP) antibodies:**

- a. Currently being explored as an RF adjunct,<sup>5-7</sup> but routine use in the pediatric setting is not indicated until the full clinical significance in this population has been established.
- b. Although pediatric studies are few, anti-CCP has been shown to have a high sensitivity and specificity for adult rheumatoid arthritis (RA).
- c. Anti-CCP-positive juvenile rheumatoid arthritis (JRA) patients are usually also RF positive, as are females with late-onset polyarthritis.<sup>7</sup>
- d. Anti-CCP positivity correlates with erosive joint disease in JIA.<sup>8</sup>

**C. Complement<sup>1,9</sup>**

The complement system is composed of a series of plasma proteins and cellular receptors that function together to mediate host defense and inflammation. Inflammatory processes may increase complement protein synthesis or increase their consumption.

**1. Total hemolytic complement level (CH<sub>50</sub>):**

- a. General measure of complement; also an acute-phase reactant
- b. Increased in the acute phase response of numerous inflammatory states
- c. Useful screening test for homozygous complement deficiency states
- d. Typically decreased in SLE

**2. C3 and C4:**

- a. Most common complement proteins assayed
- b. May be increased or decreased in rheumatic diseases, depending on stage of disease or severity
- c. Trends more instructive than isolated results

**3. Decreased levels of complement proteins:**

- a. Indicator of immune complex formation:
  - (1) Can occur in active SLE, some vasculitides, and multiple infections, including gram-negative sepsis, hepatitis, and pneumococcal infections.
  - (2) Decreased levels typically signify more severe SLE, particularly with regard to renal disease.
- b. Severe hepatic failure: Synthesis of complement proteins occurs primarily in the liver.
- c. Congenital complement deficiency, which may predispose to development of autoimmune disease.

**4. Increased levels of complement proteins:**

- a. Indicates the active phase of most rheumatic diseases (e.g., SLE, JIA, dermatomyositis)
- b. May be seen in multiple infections (e.g., hepatitis, pneumococcal pneumonia) as part of the acute-phase response

**D. Other Laboratory Studies**

**1. Urinalysis:**

- a. Renal involvement occurs in many rheumatic diseases.
- b. Findings may include proteinuria, hematuria, or casts (see Chapter 19).



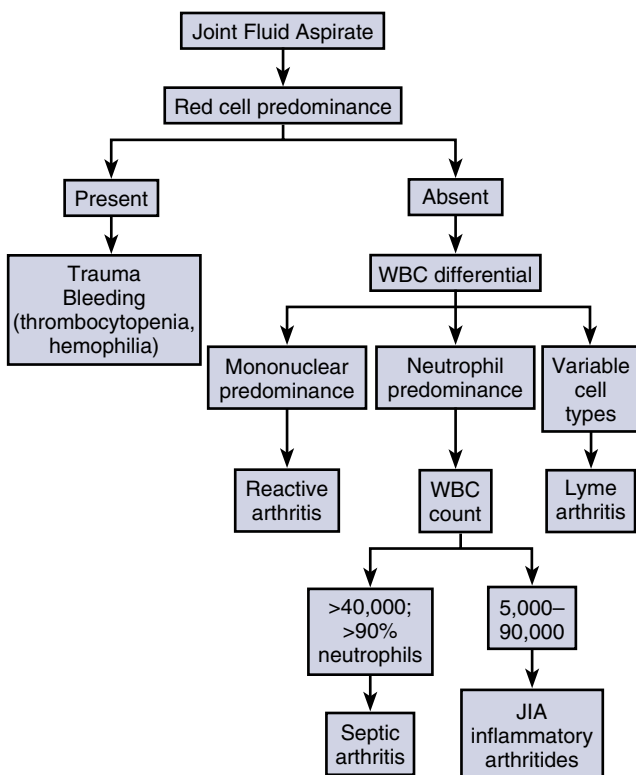
## 2. Serum muscle enzymes<sup>2</sup>:

- Including aspartate aminotransferase (AST), lactate dehydrogenase (LDH), aldolase, and creatine kinase (CK)
- Can be elevated in certain rheumatic diseases that cause muscle inflammation or destruction (e.g., dermatomyositis)

**NOTE:** Patients with chronic ongoing myositis may have an elevated CK-MB fraction (noncardiac in origin) when serum CK levels are measured.

## 3. Joint fluid analysis (Fig. 26-1)<sup>10</sup>:

- Important in the presence of an effusion, especially monoarticular disease.
- Effusion can be seen in rheumatic and other disease processes (e.g., septic arthritis).



**FIGURE 26-1**

Joint fluid analysis algorithm. JRA, Juvenile rheumatoid arthritis; WBC, white blood cell. (Data from Hay W, Levin M, Sondheimer J, et al. *Current Pediatric Diagnosis and Treatment*. 17th ed. New York: Lange Medical/McGraw-Hill, 2005.)

### III. ARTHRITIDES

#### A. Juvenile Rheumatoid Arthritis<sup>1,2,9</sup> and Juvenile Idiopathic Arthritis<sup>12</sup>

1. **Definition of arthritis:** Joint swelling or limitation/tenderness upon range of motion (ROM), lasting  $\geq 6$  weeks and not due to other identifiable cause<sup>11</sup>
2. **Diagnosis:**
  - a. Challenge of diagnosis: Children may not present with joint pain/swelling but other symptoms: morning stiffness, limp, refusal to walk, irritability, poor growth, or limb discrepancy.
  - b. Classical divisions: Based on clinical course over the first 6 months of illness in children <age 16 years, with arthritis present for at least 6 weeks.<sup>1,2</sup> Multiple classification systems exist; American College of Rheumatology (ACR) and International League of Associations for Rheumatology (ILAR) classifications are most widely used.<sup>11</sup> Divisions used here are based on ACR classification (Table 26-2).

**NOTE:** When evaluating a child with a history of chronic extremity pain (including nighttime awakenings due to pain), low white blood cell (WBC) count, and low-normal platelets, consider in the differential malignancy such as acute lymphocytic leukemia (even without blasts seen on peripheral smear). Bone marrow studies may be indicated.<sup>13</sup>

#### 3. Uveitis

Development of uveitis is often insidious and asymptomatic, so routine pediatric ophthalmology screening is required for children with JIA:

- a. **At diagnosis:** First ophthalmologic examination should be within 1 month.
- b. **Inactive disease:** Frequency of examination varies based on ANA status, disease duration, and age at diagnosis.<sup>18</sup>
- c. **Active disease:** Ophthalmologic examination every 3 months, regardless of ANA status.

#### B. Psoriatic Arthritis (PsA)<sup>14,15</sup>

1. **Classification:** Traditionally referred to as a *seronegative spondyloarthropathy*; ILAR classification considers PsA a subtype of JIA.<sup>11</sup>
2. **History of psoriasis:** Not required for diagnosis (*psoriatic arthritis sine psoriasis*):
  - a. Patients often have a first-degree relative with psoriasis.
  - b. Patients may develop skin findings months or years after arthritis onset.
3. **Presentation:**
  - a. Mostly an oligoarthritis but may be a polyarthritis or axial arthritis.
  - b.  $\pm$ Sacroiliitis, inflammatory spinal pain/stiffness, synovitis, enthesitis, or dactylitis of toes or fingers (swelling beyond joint margins, producing a so-called sausage digit), especially the distal interphalangeal (DIP) joint.
  - c. Fingernails may show onycholysis or pitting.
4. **Laboratory studies:** No specific laboratory findings suggest a diagnosis of psoriatic arthritis, although markers of inflammation (CRP, ESR) may be helpful in tracking activity of disease. RF is usually negative.

TABLE 26-2

CLASSICAL DIVISIONS OF JUVENILE IDIOPATHIC ARTHRITIS<sup>35</sup>

	Pauciarticular	Polyarticular	Systemic-Onset
Frequency of cases	60%	30%	10%
Number of joints involved (in first 6 mo)	≤4	≥5	Variable
Age predominance	Type I: preschool age Type II: 9–11 yr	2–5 yr and 10–18 yr	None
Gender ratio (female/male)	Type I: 4:1 Type II: 1:20	3:1	1:1
Involved joints	Knees and ankles	Larger joints, symmetric involvement	Any, including hips
Chronic uveitis	20% (higher with [+] ANA)	5%	Rare
Extraarticular manifestations	Uveitis	Mild fever, hepatosplenomegaly, lymphadenopathy, subcutaneous nodules	Once- to twice-daily high-spiking fevers, hepatosplenomegaly, lymphadenopathy, polyserositis, pericarditis, and characteristic macular rash
Seropositivity			
ANA	75%–85%	40%–50%	10%
RF	10% (increases with age)	75%–85%	10%
Destructive arthritis	Rare	>50%	>50%
Major morbidities	Uveitis, leg length discrepancy		Pericarditis, pleuropericarditis, secondary amyloidosis, macrophage activation syndrome*
Prognosis	Excellent apart from eyesight	Poorer prognosis with RF seropositivity and later onset	Moderate to poor

\*Macrophage activation syndrome (MAS) or reactive hemophagocytic lymphohistiocytosis: uncontrolled activation of T cells and macrophages, leading to rapid hepatic failure, encephalopathy, pancytopenia, purpura, mucosal bleeding, and renal failure. Paradoxically low erythrocyte sedimentation rate (ESR) with hypofibrinogenemia, elevated ferritin, and triglycerides, with disseminated intravascular coagulation (DIC).

ANA, Antinuclear antibody; RF, rheumatoid factor.

Modified from McMillan JA, Feigin RD, DeAngelis CD, et al. *Oski's Pediatrics*. 4th ed. Philadelphia, Lippincott Williams & Wilkins, 2006.

- 5. Radiographic findings:** Blend of destruction and proliferation on plain films.
- 6. Prognosis:** If left untreated, will result in a deforming combination of erosions and ankylosis within joints of digits.
- 7. Major morbidities:** Chronic uveitis may develop; regular screening by an ophthalmologist recommended.

## C. Reactive Arthritis<sup>2</sup>

- 1. Definition:** Diverse group of inflammatory arthritides that follow a bacterial or viral infection, particularly involving respiratory, gastrointestinal (GI), and genitourinary tracts.

2. **Onset:** Infection typically precedes development of arthritis by 1–4 weeks; ≈80% of cases are preceded by gastroenteritis.
3. **Common precipitating organisms:** *Mycoplasma*, *Chlamydia*, *Yersinia*, *Salmonella*, *Shigella*, *Campylobacter*, *Neisseria gonorrhoeae*, Epstein-Barr virus (EBV), parvovirus B19, and enteroviruses.
4. **Presentation:** Sometimes accompanied by constitutional signs and symptoms (fever, weight loss, fatigue), as well as dermatologic and ophthalmologic findings.
5. **HLA-B27:**
  - a. Strong association between HLA-B27 and susceptibility to developing reactive arthritis after an infection with a bacterial arthritogenic organism
  - b. ≈50%–65% frequency seen in reactive arthritis
6. **Laboratory studies:**
  - a. ±Evidence of systemic inflammation (leukocytosis, thrombocytosis, elevated ESR and CRP).
  - b. Autoantibodies are typically absent.
  - c. Stool cultures, serum *Chlamydia pneumoniae* and *Mycoplasma* titers, and urinary *Chlamydia* DNA probe can be helpful. Negative stool culture does not exclude diagnosis of reactive arthritis secondary to an enteric organism.
  - d. Complement-deficient patients are at risk to develop gonorrheal arthritis, so complement levels should be measured in patients likely to be infected.
  - e. Consider enterovirus, EBV, and parvovirus B19 antibody titers.
  - f. Joint fluid analysis may be helpful to distinguish septic arthritis from reactive arthritis, especially in the case of *Salmonella* infection, where either a septic or reactive arthritis may develop (see Fig. 26-1).
7. **Prognosis:** Arthritis can last weeks to months, with eventual remission or development of recurrent episodes.

## D. Management of Arthritis

1. **Pharmacologic agents**<sup>1,2,7,13</sup>: See [Formulary for dosing guidelines and Table EC 26-A for related side effects and laboratory surveillance](#)
  - a. Nonsteroidal antiinflammatory drugs (NSAIDs): First-line (e.g., naproxen, ibuprofen)
  - b. Disease-modifying antirheumatic drugs (DMARDs): Slow disease progression (e.g., methotrexate, sulfasalazine, hydroxychloroquine)
  - c. Biologic immunomodulators: Tumor necrosis factor (TNF) inhibitors (e.g., etanercept, infliximab, adalimumab); rituximab (anti-CD20); abatacept (modulates T-cell activation); and interleukin (IL)-1 receptor antagonist (anakinra, canakinumab)
  - d. Cytotoxic and immunosuppressive drugs: Cyclosporine and mycophenolate mofetil
  - e. Corticosteroids: Can be systemic or intraarticular
2. **Health maintenance**<sup>1,7,13,16,17</sup>:
  - a. Vaccines: Generally follow regular immunization schedule. Special considerations should be made for immunocompromised hosts (i.e., patients on biologic or immunosuppressive therapy; see Chapter 16). May have to postpone live viral vaccines.

TABLE EC 26-A

## ANTIARTHRITIC DRUG TOXICITY AND RECOMMENDED SURVEILLANCE

Agent	Major Side Effects	Recommended Surveillance
<b>DMARDS</b>		
Methotrexate	Abdominal discomfort, nausea, liver toxicity, bone marrow toxicity, teratogenic	Baseline CMP Q2–3 mo
Hydroxychloroquine	Retinal toxicity	Ophthalmologic monitoring Q6 mo
Sulfasalazine	Hematologic toxicity, hepatic toxicity	CBC with differential, liver enzymes and urinalysis Q2–3 mo IgG levels Q6 mo
Leflunomide	Hepatic toxicity, hematologic, mucositis, teratogenic, neuropathy	Baseline CBC and LFTs monthly for 6 mo, then Q8–12 wk
<b>CYTOTOXIC AGENTS</b>		
Azathioprine	Bone marrow, liver, and lung toxicity	CBC with differential and liver function tests every 2 weeks for the first month, then monthly. <sup>40</sup>
Cyclophosphamide	Leukopenia, thrombocytopenia, bladder toxicity, SIADH	Vitals when administering IV formulation (pretreatment with mesna) Urinalysis preinfusion and post infusion Urine output monitoring, CBC with differential days 7, 10, 14 after infusion
Cyclosporine	Hypertension, immune suppression, renal toxicity, hirsutism	Baseline renal function (BUN, urinalysis, creatinine), then monthly Hepatic enzymes, CBC with differential
<b>BIOLOGIC AGENTS</b>		
Anti-TNF agents	Opportunistic infections, drug-induced lupus, malignancy, autoantibody production	Baseline TB screening Routine CBC Routine autoantibody screening

ALT, Alanine aminotransferase; AST, aspartate aminotransferase; CBC, complete blood cell count; CMP, comprehensive metabolic panel; BUN, blood urea nitrogen; DMARD, disease-modifying antirheumatic drug; IgG, immunoglobulin G; IV, intravenous; LFTs, liver function tests; SIADH, syndrome of inappropriate antidiuretic hormone; TB, tuberculosis; TNF, tumor necrosis factor.

Modified from McMillan JA, Feigin RD, DeAngelis CD, et al. *Oski's Pediatrics*. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2006.

TABLE 26-3

## DIFFERENTIAL DIAGNOSIS FOR JOINT OR EXTREMITY PAIN

<b>Rheumatologic</b>	JIA; SLE; juvenile dermatomyositis; polyarteritis; scleroderma; Sjögren syndrome; Behçet's disease; Wegner granulomatosis; sarcoidosis; HSP; chronic recurrent multifocal osteomyelitis; juvenile ankylosing spondylitis; psoriatic arthritis
<b>Infectious</b>	Bacterial: <i>Staphylococcus aureus</i> , <i>Streptococcus pneumoniae</i> , <i>Neisseria gonorrhoeae</i> , <i>Haemophilus influenzae</i> Viral: parvovirus, rubella, mumps, EBV, hepatitis B Fungal Other: spirochetes, mycobacterial, endocarditis, Lyme
<b>Immunodeficiencies</b>	Hypogammaglobulinemia; IgA deficiency; HIV
<b>Congenital and Metabolic</b>	Gout and pseudogout; mucopolysaccharidoses; hypothyroidism or hyperthyroidism; vitamin C or D deficiency; connective tissue disease; lysosomal storage diseases: Fabry and Farber; familial mediterranean fever
<b>Bone and Cartilage</b>	Trauma; patellofemoral syndrome; osteochondritis dissecans and avascular necrosis; SCFE; hypertrophic osteoarthropathy
<b>Inflammatory and Reactive</b>	Kawasaki syndrome; IBD; acute rheumatic fever; reactive arthritis; toxic synovitis; serum sickness
<b>Neurologic and Pain Syndromes</b>	Peripheral neuropathy; carpal tunnel syndrome; Charcot joints; fibromyalgia; depression with somatization; reflex sympathetic dystrophy
<b>Neoplastic</b>	Leukemia and lymphoma; neuroblastoma; histiocytosis; synovial tumors Bone tumors: osteosarcoma, Ewing sarcoma, osteoid osteoma

IBD, Inflammatory bowel disease; EBV, Epstein-Barr virus; HIV, human immunodeficiency virus; HSP, Henoch-Schönlein purpura; JIA, juvenile idiopathic arthritis; SCFE, slipped capital femoral epiphysis; SLE, systemic lupus erythematosus. Modified from Kliegman RM, Stanton BF, St. Geme JW, et al. *Nelson Textbook of Pediatrics*. 19th ed. Philadelphia: Saunders Elsevier, 2011.

- Prevention or minimization of osteopenia: Adequate calcium and vitamin D intake and weight-bearing activities.
- Physical and occupational therapy: Important in maintaining joint ROM and strength of associated muscle groups, as well as decreasing pain and preventing joint deformity and contractures.
- Orthopedic surgery: Necessary in some cases for pain control, improvement in function, or contracture.

## E. Differential Diagnosis

See Table 26-3 for differential diagnosis of joint/extremity pain.

## IV. SYSTEMIC LUPUS ERYTHEMATOSUS

An episodic multisystem autoimmune disease characterized by inflammation of blood vessels and connective tissue. Apart from drug-induced SLE, the etiology remains unknown.

### A. American College of Rheumatology Classification Criteria (Table 26-4)

These are not strict *diagnostic* criteria, but *classification* criteria for research purposes. Use caution when applying them to pediatric and international/multiethnic patients; few studies validate ACR criteria for these populations.<sup>19,20</sup>

**Note:** In 2012 the SLICC criteria were published, but they are still being investigated.

TABLE 26-4

**1997 UPDATE OF THE 1982 AMERICAN COLLEGE OF RHEUMATOLOGY REVISED CRITERIA FOR CLASSIFICATION OF SYSTEMIC LUPUS ERYTHEMATOSUS**

Criterion	
Malar rash	Fixed erythema (flat or raised) over malar eminences, tending to spare nasolabial folds; telangiectasias
Discoid rash	Erythematous raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions
Photosensitivity	Rash due to unusual reaction to sunlight (by patient history or physician observation)
Oral ulcers	Oral or nasopharyngeal ulceration, usually painless, observed by physician
Nonerosive arthritis	Involving two or more peripheral joints, characterized by tenderness, swelling, or effusion
Pleuritis or pericarditis	1. Pleuritis: history of pleuritic pain or rubbing heard by physician, or evidence of pleural effusion AND/OR 2. Pericarditis: documented by electrocardiogram or rub or evidence of pericardial effusion
Renal disorder	1. Persistent proteinuria > 0.5 g/day or > 3+ if quantitation not performed AND/OR 2. Cellular casts: may be red cell, hemoglobin, granular, tubular, or mixed
Neurologic disorder	Seizures or psychosis: in the absence of offending drugs, hypertension, or known metabolic derangements
Hematologic disorder	1. Hemolytic anemia with reticulocytosis AND/OR 2. Leukopenia: <4000/ $\mu$ L on $\geq$ two occasions AND/OR Lymphopenia: <1500/ $\mu$ L on $\geq$ two occasions AND/OR 3. Thrombocytopenia: <100,000/ $\mu$ L in the absence of offending drugs
Autoimmune markers	1. Anti-DNA: antibody to native DNA in abnormal titer AND/OR 2. Anti-Smith (Sm): presence of antibody to Sm nuclear antigen
Positive antinuclear antibody	An abnormal titer of antinuclear antibody by immunofluorescence or an equivalent assay at any point in time in the absence of drugs

Data from <http://www.rheumatology.org/>, which was modified from Tan E, Cohen AS, Fries JF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum.* 1982;25:1271-1277.

**B. Clinical Features and Management of SLE****1. Diagnosis:**

- Most often based on meeting 4 or more of the 11 classification criteria.
- Do not exclude the possibility of an SLE diagnosis for a pediatric patient who does not fully meet these criteria.
- Majority of pediatric patients with *incomplete SLE* (<4 criteria) will likely completely fulfill these criteria in subsequent years.

**2. Epidemiology:**

- Females more commonly affected; onset usually at age 9–15 years (median age, 12 years).<sup>19</sup>
- African Americans and Asian Americans more commonly affected than whites.<sup>1</sup>

**3. Laboratory studies and surveillance<sup>1,15</sup>:**

- a. CBC with differential and direct Coombs.
- b. Urinalysis and serum creatinine: Of note, renal disease is the leading cause of death in lupus patients. See Table EC 26-B for World Health Organization (WHO) classification of SLE nephritis.<sup>21</sup>
- c. ESR or CRP: May be increased with active disease; CRP levels may not correlate with disease activity.<sup>22</sup>
- d. Complement levels (C3, C4): Serial levels most useful. Congenital complement deficiencies may also be seen in SLE, especially in males. Decreasing complement levels may indicate renal disease.
- e. Autoantibodies (see Table 26-1)<sup>1</sup>:
  - (1) ANA: Most patients with positive ANA do not have SLE, but almost all patients with SLE have positive ANA.<sup>5</sup>
  - (2) Anti-ds (double-stranded) DNA: Highly specific for SLE, seen in about 60% of patients. Titers rise/fall depending on disease activity and usually increase during development of lupus nephritis. Not associated with discoid or subacute cutaneous lupus.<sup>5</sup>
  - (3) Anti-Sm: Highly specific for SLE; seen in ≈10%–30% of patients.

**4. Treatment<sup>1</sup>:**

- a. NSAIDs: Targeted to treat arthralgia and arthritis (use with caution; lupus patients more susceptible to renal toxicity with these agents).
- b. Hydroxychloroquine: treats milder manifestations (e.g., skin lesions, arthritis) and may lower lipid levels, decreasing risk for thromboembolic disease.
- c. Corticosteroids: Used to treat symptoms and decrease autoantibody production.
- d. Cytotoxic therapy: Reserved for more severe cases. Cyclophosphamide is used in patients with lupus nephritis, vasculitis, pulmonary hemorrhage, or central nervous system involvement.
- e. DMARDs: Methotrexate, cyclosporine, mycophenolate mofetil.
- f. Biologics: Agents that target cytokine production; includes anti-CD20/22 monoclonal antibodies (i.e., rituximab).

**C. Drug-Induced SLE<sup>1,2</sup>****1. Pathogenesis:**

- a. Inciting drugs (including but not limited to): hydralazine, minocycline, ethosuximide, doxycycline, procainamide, isoniazid, chlorpromazine, phenytoin, carbamazepine
- b. Usually resolves with discontinuation of drug

**2. Clinical and laboratory features:**

- a. Most frequent clinical manifestations are cutaneous and pleuropericardial involvement.
- b. Often associated with antihistone antibodies.

**D. Neonatal SLE<sup>1,21</sup>**

- 1. **Pathogenesis:** Neonates born to mothers with active SLE can develop a transient lupus-like syndrome in the perinatal period. Transplacental



TABLE EC 26-B

**WORLD HEALTH ORGANIZATION CLASSIFICATION OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) NEPHRITIS**

Class	Histopathology	Description
I	Normal kidneys	Minimal to no detectable changes
II	Mesangial proliferative glomerulonephritis	Mesangial hypercellularity or mesangial matrix expansion
III	Focal proliferative glomerulonephritis	<50% of glomeruli involved, with intracapillary and extracapillary cell proliferation, necrosis
IV	Diffuse proliferative glomerulonephritis	Similar to class III but involves more glomerular surface area and >50% of glomeruli
V	Membranous glomerulonephritis	No mesangial, endothelial, or epithelial cell proliferation; thickening of capillary walls
VI	Advanced sclerosing glomerulonephritis	>90% of glomeruli globally sclerosed

Modified from McMillan JA, Feigin RD, DeAngelis CD, et al. *Oski's Pediatrics*. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2006.

passage of anti-Ro (anti-SS-A) and anti-La (anti-SS-B) (also seen in Sjögren syndrome) mediate disease process. Mothers are often asymptomatic but carry antibodies, so mothers are routinely screened for SS-A and SS-B.

## 2. **Clinical and laboratory features:**

- a. Thrombocytopenia, hemolytic anemia.
- b. Inflammatory features of neonatal lupus will resolve within 6 months as maternal autoantibodies are cleared.
- c. Congenital heart block (associated with anti-Ro): *Permanent* condition; usually requires placement of a pacemaker.
- d. Common cause of hydrops likely secondary to heart block or Coombs antibody-mediated immune anemia.

## V. VASCULITIS

### A. General (Table 26-5)<sup>28</sup>

1. **Definition:** Inflammation of a blood vessel wall. Systemic vasculitis syndromes, although rare, are a concern in childhood.
2. **Clinical presentation:** Variable, ranging from rash or fever of unknown origin to progressive multisystem failure.<sup>23</sup>
3. **Initial laboratory tests:** CBC, basic metabolic panel, liver function tests, acute phase reactants, stool guaiac, and complete urinalysis.
4. **Diagnosis:**
  - a. Small vessel vasculitis: Confirmed by biopsy. Magnetic resonance angiography (MRA) may also be helpful, but a negative test does not rule out disease.
  - b. Medium-large vessel vasculitis: MRA.

### B. Henoch-Schönlein Purpura (HSP)<sup>1,2,24,25</sup>

1. **Epidemiology:**
  - a. Most common small-vessel vasculitis in children
  - b. More frequent in males than females
  - c. Typical age of onset 2–7 years
  - d. History of viral upper respiratory infection several weeks preceding onset of illness in half to two thirds of cases
2. **Presentation<sup>2,19–21</sup>:**
  - a. Nonthrombocytopenic palpable purpura:
    - (1) Most common and frequently presenting feature.
    - (2) Evolution of rash: Urticarial lesions progress to a maculopapular rash, followed by purpuric lesions involving ankles, buttocks, and elbows, beginning on lower extremities but can involve entire body.
    - (3) New lesions can appear over 2–4 weeks, leaving a mixed-stage appearance.
  - b. Migratory polyarthritis and/or polyarthralgias:
    - (1) Presenting feature in 25% of cases: Very tender and painful periarticular joint swelling of ankles and knees (most often), without effusion.

TABLE 26-5

## CHILDHOOD VASCULITIS SYNDROMES

Vessel Size	Vasculitis Syndrome	Clinical and Distinguishing Features
Large arteries	Takayasu arteritis	Aortic arch involvement leading to aneurysms, thrombosis, and stenosis Predominantly seen in young women Hypertension is most common sign
Aorta and large branches directed toward major body regions	Giant cell (temporal arteritis)	Granulomatous inflammation of aorta and major branches, with predilection for extracranial branches of carotid artery
Medium-sized arteries	Kawasaki disease	Arteritis including large, medium, and small arteries; associated with mucocutaneous lymph node syndrome (see Chapter 7)
Renal, hepatic, coronary, and mesenteric arteries	Polyarteritis nodosa	Cutaneous lesions include livedo reticularis, tender nodules, purpura Hypertension, renal failure, abdominal pain, intestinal infarction, and cerebrovascular accidents are common complications
Small arterioles and venules	Microscopic polyangiitis	Rare in pediatrics p-ANCA or myeloperoxidase (MPO) positive Glomerulonephritis and pulmonary capillaritis Associated with streptococcal infection or URIs
Venules, capillaries, arterioles, and intra-parenchymal distal arteries	Henoch-Schönlein purpura	Most common pediatric vasculitis IgA-dominant immune deposits, palpable purpura involving buttocks and lower extremities, colicky abdominal pain, arthralgias/arthritis
	Wegener granulomatosis	Necrotizing granulomatous vasculitis of small and medium-sized vessels Presents with respiratory tract and kidney involvement c-ANCA or proteinase-3 (PR3) positive May also involve medium-sized vessels
	Churg-Strauss syndrome	Eosinophil-rich and granulomatous inflammation involving respiratory tract; associated with asthma

cANCA, Cytoplasmic antineutrophil cytoplasmic antibody; IgA, immunoglobulin A; pANCA, perinuclear antineutrophil cytoplasmic antibody; URI, upper respiratory infection.

Modified from Kliegman RM, Behrman RE, Jenson HB, et al. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia: Saunders Elsevier, 2007; Cassidy J, Petty R. *Textbook of Pediatric Rheumatology*. 5th ed. Philadelphia: WB Saunders, 2005; Kim S, Dedeoglu F. Update on pediatric vasculitis. *Curr Opin Pediatr*. 2005;17:695-702; and Dillon M, Ozen S. A new international classification of childhood vasculitis. *Pediatr Nephrol*. 2006;21:1219-1222.

- (2) Joint involvement is transient with no permanent deformities.
- c. Abdominal pain:
  - (1) Colicky in nature, secondary to hemorrhage and edema of small intestine.
  - (2) Intussusception results in about 2% of cases (usually ileoileal).
  - (3) Stool can be guaiac positive without obvious signs of intestinal bleeding.
- d. Glomerulonephritis:
  - (1) Occurs in 20%–60% of patients; may develop months after onset or before development of rash
  - (2) Renal biopsy: Typically consistent with IgA nephropathy, but crescentic glomerulonephritis may also be seen.
  - (3) More common in males, patients with GI bleeding, factor VIII activity <80%, and in patients <age 4 years<sup>27</sup>
- e. Other features: Acute scrotal inflammation (2%–38% of male patients), dorsal edema of feet, occult pulmonary involvement
- 3. **Diagnosis:** Based on clinical characteristics<sup>2,23,24</sup>
- 4. **Laboratory findings:** Can help exclude other diagnoses and illuminate specific organ involvement:
  - a. Hematologic: Normal to elevated platelet count, normal platelet function tests and bleeding time, normal coagulation studies.
  - b. Urinalysis:  $\pm$ proteinuria and hematuria, but casts uncommon.
  - c. Antibodies: IgA levels may be elevated, especially in acute phase of disease.
  - d. Stool guaiac: May be positive.
  - e. Anti-streptolysin O titer: May be elevated.
  - f. Throat culture may be positive for group A  $\beta$ -hemolytic streptococcus, warranting antibiotic treatment.
- 5. **Treatment**<sup>23,24</sup>:
  - a. Supportive care: Adequate hydration, analgesia for joint pain.
  - b. Monitor vital signs because of GI bleeding and renal involvement.
  - c. Serial urinalyses at routine office visits.
  - d. Consider steroids, especially if GI and renal systems involved.
  - e. Prolonged immunosuppression may be necessary for renal disease (cyclophosphamide or azathioprine).
- 6. **Prognosis:** Typically self-limited course, but may recur in a minority (10%–20%) of cases.

### **C. Juvenile Dermatomyositis**<sup>1,2,9,35-38</sup>

- 1. **Pathogenesis:**
  - a. Nonsuppurative vasculitis with inflammation of skin, GI tract, and striated muscle.
  - b. Unlike adult-onset form, juvenile dermatomyositis is not related to malignancy.
- 2. **Epidemiology:**
  - a. One study found the incidence to be 3.2 cases per million children per year; female/male ratio of 2.3:1.
  - b. Peak age of onset for juvenile form is 5–14 years.

**3. Presentation:**

- a. Constitutional: Fever, fatigue, weight loss.
- b. Musculoskeletal: Symmetric proximal muscle pain or weakness involving shoulder and pelvic girdles.
- c. Dermatologic: Heliotropic rash involving upper eyelids (or malar rash); Gottron papules (thickened, erythematous, scaly rash on extensor surfaces of elbows, knees, metacarpophalangeal and proximal interphalangeal joints). Dystrophic cutaneous calcifications or photosensitivity may be present.  
(1) Dermatologic symptoms are required to diagnose dermatomyositis.
- d. Respiratory: Dyspnea/tachypnea may be present (restrictive lung disease due to respiratory muscle weakness), indicating more severe disease and poorer prognosis.
- e. Other: Dysphagia, periorbital edema, nailfold or eyelid rim capillary abnormalities (dilation, aneurysms, dropout).

**4. Laboratory studies:**

- a. Elevated muscle enzymes: AST, ALT, CK, LDH, and aldolase; may be normal at diagnosis.<sup>37</sup>
- b. ANA may be positive; acute-phase reactants (ESR, CRP) are often normal.<sup>36</sup>

**5. Diagnosis:**

- a. Muscle biopsy: Gold standard for definitive diagnosis.
- b. MRI: Often used to demonstrate affected areas: T1-weighted images may show fibrosis, atrophy, and fatty infiltration; T2-weighted images may demonstrate active myositis.

**VI. GRANULOMATOUS DISEASE****A. Differential Diagnosis<sup>30,31</sup>**

- 1. **Infectious causes:** Tuberculosis, atypical mycobacteria, including leprosy, histoplasmosis, coccidioidomycosis, brucellosis, chlamydia, tularemia, treponemal organisms, leishmaniasis, toxoplasmosis
- 2. **Environmental exposures:** Hypersensitivity pneumonitis, berylliosis, silicosis, other metals (aluminum and titanium), talc
- 3. **Immune dysregulation:** Wegener granulomatosis, primary biliary cirrhosis, Churg-Strauss syndrome, sarcoidosis, Takayasu arteritis, Crohn's disease, chronic granulomatous disease
- 4. **Other:** Malignancy, foreign bodies, medications

**B. Sarcoidosis<sup>2,31-34</sup>**

- 1. **Pathophysiology:** Multisystem infiltrative noncaseating granulomatous disease of unknown etiology
- 2. **Epidemiology:**
  - a. Before puberty (very rare): Primarily affects caucasians.
  - b. During and after puberty: Predominantly affects African Americans.
  - c. Incidence increases with age, peaking between 20 and 40 years of age.
  - d. Males and females affected equally.

**3. Two forms of pediatric sarcoidosis:**

- a. Before puberty (usually <age 4): May be familial; dominated by skin, musculoskeletal, and eye involvement
- b. During or after puberty: Very similar to adult disease; dominated by lung, lymphatic, eye, and systemic involvement

**4. Presentation:** Lymphadenopathy is most common initial manifestation

- a. General: Weight loss, fever, anorexia, fatigue
  - b. Musculoskeletal: Usually only seen in young children. Tenosynovitis and polyarthritis, mostly of wrists, knees, and ankles<sup>32</sup>
  - c. Pulmonary: Dyspnea on exertion, chest pain, chronic dry cough, wheezing or stridor, bilateral hilar lymphadenopathy with or without parenchymal disease on chest x-ray or computed tomography (CT), and restrictive pattern with impaired gas exchange on pulmonary function tests
  - d. Ophthalmologic: Bilateral uveitis (anterior, posterior, or panuveitis), band keratopathy, synechiae, iris nodules, cataracts, glaucoma, chorioretinitis, conjunctivitis, papilledema
  - e. Dermatologic: Erythema nodosum, plaques, maculopapules, subcutaneous nodules
  - f. Lymphatic: Hilar, mediastinal, and mobile, nontender peripheral lymphadenopathy
  - g. Neurologic: Headache, seizures, cranial nerve (CN VI, VII, VIII) palsies, pseudotumor cerebri, obstructive hydrocephalus, hemiparesis:
    - (1) CN VII palsy: Most common neurologic manifestation in adolescent/adult form.<sup>33</sup>
    - (2) Magnetic resonance imaging (MRI) may show mass lesion(s), periventricular white matter lesions, nodular or diffuse leptomeningeal enhancement.<sup>34</sup>
  - h. Cardiovascular: Arrhythmia, valvular disease, vasculitis of any size vessel
  - i. Renal: Renal failure (due to hypercalcemia or parenchymal infiltration) and nephrolithiasis
  - j. GI: Hepatosplenomegaly, elevated transaminases, hyperbilirubinemia due to parenchymal and biliary tree infiltration, parotitis, and rarely intestinal obstruction with rectal prolapse
  - k. Endocrine: Pituitary dysfunction (e.g., diabetes insipidus, hypercalcemia)
- 5. Laboratory studies:**
- Nonspecific:
- a. Hypercalcemia (due to pulmonary alveolar macrophage hydroxylation of vitamin D to active 1,25 dihydroxy form).
  - b. Elevated serum angiotensin-converting enzyme (ACE; produced by epithelial cells in granulomata).
  - c. Leukopenia, increased immunoglobulins, and eosinophilia are common.
- 6. Initial evaluation:**
- Thorough history and physical examination, chest x-ray or CT, complete metabolic panel, pulmonary function testing, electrocardiogram, and ophthalmologic (slit-lamp) examination

**7. Diagnosis:** Biopsy demonstrating noncaseating granulomas in absence of other known cause

**8. Treatment:** Glucocorticoids standard; methotrexate, azathioprine secondary alternatives

## VII. OTHER RHEUMATIC DISEASES

A. Scleroderma<sup>2,26</sup>

1. **Definition/classifications:** *Scleroderma* means “hard skin”; divided into localized and systemic
2. **Localized (limited) scleroderma:**
  - a. More common than systemic disease.
  - b. Clinical manifestations:
    - (1) Morphea: Discrete cutaneous lesions of varying size, characterized by hypopigmentation and induration surrounded by hyperpigmented skin. Erythema and inflammatory edema often are present at margins of lesions. Lesions may enlarge or coalesce.
    - (2) Linear morphea: Typically present during the first 2 decades of life. Linear involvement of head, trunk, or extremities. Often, underlying muscle and bone fibrosis occurs unilaterally, leading to localized growth abnormalities, contractures, and hemiatrophy.
  - c. Laboratory findings: ANA positive in ≈50%. Anticentromere or Scl-70 rarely present.
  - d. Treatment: Topical emollients and glucocorticoids may be effective. Some studies support systemic antibiotics to treat morphea.
  - e. Prognosis: Multiple disease exacerbations of varying duration, although lesions tend to regress slowly over time. Patients with linear scleroderma may have visceral disease with progression of deep tissue involvement.
3. **Diffuse cutaneous systemic scleroderma (DCSS):**
  - a. Definition: Chronic multisystem connective tissue disease, characterized by fibrous thickening and hardening of skin, with fibrous degenerative changes in synovium, digital arteries, and internal organs (GI tract, heart, lungs, kidneys, esophagus).
  - b. Clinical manifestations:
    - (1) Often initially presents with Raynaud phenomenon (blanching, cyanosis, and erythema occurring spontaneously or in response to cold or stress), cutaneous telangiectasias, and thinning/tightening of skin
    - (2) Musculoskeletal: Morning stiffness and pain in small joints
    - (3) GI: Heartburn, progressive dysphagia from esophagitis, ulceration, strictures
    - (4) Cardiac: Pericardial effusions resulting in tamponade (primary cause of morbidity), cardiac anoxia from a Raynaud-like phenomenon of coronary arteries leading to myocardial fibrosis
    - (5) Pulmonary: Vascular and parenchymal involvement resulting in pulmonary fibrosis, right ventricular failure
    - (6) Renal: Renovascular disease leading to nephropathy with proteinuria and often systemic hypertension
  - c. Treatment: No uniformly effective therapy exists. Management principles as follows:
    - (1) Supportive care: Skin care, NSAIDs, ensuring warm ambient temperatures

- (2) Disease process–modifying therapy: Immunosuppressants, colchicine (inhibits fibroproliferative process), D-penicillamine (breakdown of collagen cross-linkage)
- (3) Management of complications (e.g., ACE inhibitors for renal disease)
- d. Prognosis: Generally poor; dictated by progression and extent of cardiac, pulmonary, and renal disease

## B. Behçet Disease<sup>1</sup>:

1. **Characteristics:** Variable course with disease-free periods and exacerbations:
  - a. Oral ulcers: Most consistent symptom; painful, shallow, usually <1 cm diameter, surrounded by erythema; develop on tongue, lips, buccal mucosa, and gingiva; last days to weeks and heal without scarring.
  - b. Genital ulcers: Similar to oral ulcers; may result in scarring; found on labia, scrotum, and penis.
  - c. Cutaneous pathergy: Traumatic injury (e.g., needlestick) results in development of a sterile pustule 24–48 hours later.
  - d. Ophthalmologic: Anterior or posterior uveitis, retinal vasculitis; more common in adults but often more severe in children; may result in blindness.
  - e. Arthritis: Usually recurrent, asymmetric, polyarticular, and involves large joints.
  - f. Other dermatologic findings: Erythema nodosum, papulopustular lesions, pseudofolliculitis, acneiform nodules.
  - g. Others: GI include abdominal pain, dyspepsia, and mucosal ulcers. Neurologic include meningoencephalitis, cranial nerve palsies, and psychosis; usually occur in advanced disease. Rarely fever, orchitis, myositis, pericarditis, nephritis, splenomegaly, and amyloidosis. Increased risk for thrombophlebitis and venous thrombosis.
2. **Diagnosis:** Based on International Study Group criteria<sup>39</sup>:
  - a. Recurrent oral ulcers: At least 3 times in a 12-month period
  - b. Two or more of the following: Recurrent genital ulcers, eye lesions, other skin lesions, positive skin pathergy test
3. **Treatment:** Corticosteroids, colchicine, anti-TNF- $\alpha$  agents, chlorambucil, azathioprine, cyclosporine, tacrolimus, and interferon alfa-2a have been used. Symptomatic treatment of oral ulcers includes rinses with tetracycline, topical anesthetics, and chlorhexidine.

## C. Sjögren Syndrome<sup>2</sup>

1. **Characteristics:**
  - a. Clinical: Keratoconjunctivitis sicca (dry eyes secondary to decreased tear production by lacrimal glands) and xerostomia (dry mouth from decreased salivary gland production)
  - b. Serologic: Positive autoantibodies to nuclear antigens Ro/SS-A and La/SS-B
  - c. Classifications:
    - (1) Primary Sjögren syndrome: Disease present in isolation
    - (2) Secondary Sjögren syndrome: Associated with a connective tissue disease (often SLE)



**2. Clinical manifestations:**

- a. Oropharyngeal: Bilateral parotid swelling, dependence on liquids to aid in swallowing dry foods; severe dental caries
- b. Ophthalmologic: Photophobia or eye irritation, optic neuropathy
- c. Systemic: Interstitial pneumonitis, interstitial nephritis, myositis, splenic vasculitis, Hashimoto thyroiditis

**3. Pathology/laboratory findings:**

- a. Histology: Widespread lymphocytic infiltrates in salivary and lacrimal glands, with secondary atrophy and obliteration of secretory acini; proliferation of ductal lining cells to form epimyoeplithelial islands (particularly in salivary glands).
- b. Laboratory findings: Polyclonal hypergammaglobulinemia, high-titer RF, ANAs directed to Ro/SS-A and La/SS-B. Positive Schirmer test indicates deficient tear flow.

**4. Treatment:**

- a. Systemic treatment: NSAIDs and glucocorticoids
- b. Management of sicca: Artificial tears, nasal saline douches, sour lemon drops (stimulate salivation), pilocarpine tablets

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## PART III

## REFERENCE



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# Blood Chemistries and Body Fluids

*Branden Engorn, MD, and Jamie Flerlage, MD*

Determining normal reference ranges of laboratory studies in pediatric patients poses some major challenges. Available literature is often limited because of the small sample sizes of patients in many studies that have been used to derive these suggested normal ranges. **Please use great caution and be aware of this limitation when interpreting pediatric laboratory studies.**

The values that follow are compiled from both published literature and the Johns Hopkins Hospital Department of Pathology. Normal values vary with the analytic method used. Consult your laboratory for its analytic method and range of normal values and for less commonly used parameters, which are beyond the scope of this text. Additional normal laboratory values may be found in Chapters 10, 14, and 15.

A special thanks to Lori Sokoll, PhD, and Athena Kantartzis, PhD, for their guidance in preparing this chapter.

## I. REFERENCE VALUES (TABLE 27-1)

TABLE 27-1

### REFERENCE VALUES

	Conventional Units	SI Units
<b>ALANINE AMINOTRANSFERASE (ALT)<sup>1,2</sup></b>		
(Major sources: Liver, skeletal muscle, and myocardium)		
Infant <12 mo	13–45 U/L	13–45 U/L
1–3 yr	5–45 U/L	5–45 U/L
4–6 yr	10–25 U/L	10–25 U/L
7–9 yr	10–35 U/L	10–35 U/L
10–11 yr		
Female	10–30 U/L	10–30 U/L
Male	10–35 U/L	10–35 U/L
12–13 yr		
Female	10–30 U/L	10–30 U/L
Male	10–55 U/L	10–55 U/L
14–15 yr		
Female	5–30 U/L	5–30 U/L
Male	10–45 U/L	10–45 U/L
>16 yr		
Female	5–35 U/L	5–35 U/L
Male	10–40 U/L	10–40 U/L

*Continued*

TABLE 27-1

## REFERENCE VALUES (Continued)

	Conventional Units	SI Units
<b>ALBUMIN</b>		
(See Proteins)		
<b>ALDOLASE<sup>3</sup></b>		
(Major sources: Skeletal muscle and myocardium)		
10–24 mo	3.4–11.8 U/L	3.4–11.8 U/L
2–16 yr	1.2–8.8 U/L	1.2–8.8 U/L
Adult	1.7–4.9 U/L	1.7–4.9 U/L
<b>ALKALINE PHOSPHATASE<sup>4</sup></b>		
(Major sources: Liver, bone, intestinal mucosa, placenta, and kidney)		
Infant	150–420 U/L	150–420 U/L
2–10 yr	100–320 U/L	100–320 U/L
Adolescent male	100–390 U/L	100–390 U/L
Adolescent female	100–320 U/L	100–320 U/L
Adult	30–120 U/L	30–120 U/L
<b>AMMONIA<sup>2</sup></b>		
(Heparinized venous specimen on ice analyzed within 30 min)		
Newborn	90–150 mcg/dL	64–107 μmol/L
0–2 wk	79–129 mcg/dL	56–92 μmol/L
Infant/child	29–70 mcg/dL	21–50 μmol/L
Adult	15–45 mcg/dL	11–32 μmol/L
<b>AMYLASE<sup>15</sup></b>		
(Major sources: Pancreas, salivary glands, and ovaries)		
0–14 days	3–10 U/L	3–10 U/L
15 days–13 wk	2–22 U/L	2–22 U/L
13 wk–1 yr	3–50 U/L	3–50 U/L
>1 yr	25–101 U/L	25–101 U/L
<b>ANTINUCLEAR ANTIBODY (ANA)<sup>2</sup> IMMUNOFLOURESCENCE ASSAY (IFA)</b>		
Negative	<1:40	
Patterns with clinical correlation:		
Centromere: CREST*		
Nucleolar: Scleroderma		
Homogeneous: Systemic lupus erythematosus (SLE)		
<b>ANTISTREPTOLYSIN O TITER<sup>5</sup></b>		
(Fourfold rise in paired serial specimens is significant.)		
Newborn	Similar to mother's value	
6–24 mo	≤50 Todd units/mL	
2–4 yr	≤160 Todd units/mL	
≥5 yr	≤330 Todd units/mL	

TABLE 27-1

## REFERENCE VALUES (Continued)

	Conventional Units	SI Units		
<b>ASPARTATE AMINOTRANSFERASE (AST)<sup>2</sup></b>				
(Major sources: Liver, skeletal muscle, kidney, myocardium, and erythrocytes)				
0–10 days	47–150 U/L	47–150 U/L		
10 days–24 mo	9–80 U/L	9–80 U/L		
>24 mo				
Female	13–35 U/L	13–35 U/L		
Male	15–40 U/L	15–40 U/L		
<b>BICARBONATE<sup>2,4</sup></b>				
Newborn	17–24 mEq/L	17–24 mmol/L		
Infant	19–24 mEq/L	19–24 mmol/L		
2 mo–2 yr	16–24 mEq/L	16–24 mmol/L		
>2 yr	22–26 mEq/L	22–26 mmol/L		
<b>BILIRUBIN (TOTAL)<sup>4,6</sup></b>				
(Please see Chapter 18 for more complete information about neonatal hyperbilirubinemia and acceptable bilirubin values.)				
Cord:				
Term and preterm	<2 mg/dL	<34 μmol/L		
0–1 days:				
Term and preterm	<8 mg/dL	<137 μmol/L		
1–2 days:				
Preterm	<12 mg/dL	<205 μmol/L		
Term	<11.5 mg/dL	<197 μmol/L		
3–5 days:				
Preterm	<16 mg/dL	<274 μmol/L		
Term	<12 mg/dL	<205 μmol/L		
Older infant:				
Preterm	<2 mg/dL	<34 μmol/L		
Term	<1.2 mg/dL	<21 μmol/L		
Adult	<1.5 mg/dL	<20.5 μmol/L		
<b>BILIRUBIN (CONJUGATED)<sup>2–4</sup></b>				
Neonate	<0.6 mg/dL	<10 μmol/L		
Infants/children	<0.2 mg/dL	<3.4 μmol/L		
<b>BLOOD GAS, ARTERIAL (BREATHING ROOM AIR)<sup>2</sup></b>				
	pH	Pao <sub>2</sub> (mmHg)	Paco <sub>2</sub> (mmHg)	HCO <sub>3</sub> <sup>–</sup> (mEq/L)
Cord blood	7.28 ± 0.05	18.0 ± 6.2	49.2 ± 8.4	14–22
Newborn (birth)	7.11–7.36	8–24	27–40	13–22
5–10 min	7.09–7.30	33–75	27–40	13–22
30 min	7.21–7.38	31–85	27–40	13–22
60 min	7.26–7.49	55–80	27–40	13–22
1 day	7.29–7.45	54–95	27–40	13–22
Child/adult	7.35–7.45	83–108	32–48	20–28

Continued



TABLE 27-1

REFERENCE VALUES (Continued)

BLOOD GAS, ARTERIAL (BREATHING ROOM AIR)<sup>2</sup>

pH	Pao <sub>2</sub> (mmHg)	Paco <sub>2</sub> (mmHg)	HCO <sub>3</sub> <sup>-</sup> (mEq/L)
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**NOTE:** Venous blood gases can be used to assess acid-base status, not oxygenation. Pco<sub>2</sub> averages 6–8 mmHg higher than Paco<sub>2</sub>, and pH is slightly lower. Peripheral venous samples are strongly affected by the local circulatory and metabolic environment. Capillary blood gases correlate best with arterial pH and moderately well with Paco<sub>2</sub>.

	Conventional Units	SI Units
<b>C-REACTIVE PROTEIN</b> <sup>4</sup>	0–0.5 mg/dL	

**CALCIUM (TOTAL)**<sup>2</sup>

Premature neonate	6.2–11 mg/dL	1.55–2.75 mmol/L
0–10 days	7.6–10.4 mg/dL	1.9–2.6 mmol/L
10 days–24 mo	9–11 mg/dL	2.25–2.75 mmol/L
24 mo–12 yr	8.8–10.8 mg/dL	2.2–2.7 mmol/L
12–18 yr	8.4–10.2 mg/dL	2.1–2.55 mmol/L

**CALCIUM (IONIZED)**<sup>3</sup>

0–1 mo	3.9–6.0 mg/dL	1.0–1.5 mmol/L
1–6 mo	3.7–5.9 mg/dL	0.95–1.5 mmol/L
1–18 yr	4.9–5.5 mg/dL	1.22–1.37 mmol/L
Adult	4.75–5.3 mg/dL	1.18–1.32 mmol/L

**CARBON DIOXIDE (CO<sub>2</sub> CONTENT)**<sup>2</sup>

(See Blood Gas, Arterial)

**CARBON MONOXIDE (CARBOXYHEMOGLOBIN)**

Nonsmoker	0.5%–1.5% of total hemoglobin
Smoker	4%–9% of total hemoglobin
Toxic	20%–50% of total hemoglobin
Lethal	>50% of total hemoglobin

	Conventional Units	SI Units
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**CHLORIDE (SERUM)**<sup>3</sup>

0–6 mo	97–108 mEq/L	97–108 mmol/L
6–12 mo	97–106 mEq/L	97–106 mmol/L
Child/adult	97–107 mEq/L	97–107 mmol/L

**CHOLESTEROL**

(See Lipids)

**CREATINE KINASE (CREATINE PHOSPHOKINASE)**<sup>2</sup>

(Major sources: Myocardium, skeletal muscle, smooth muscle, and brain)

Newborn	145–1,578 U/L	145–1578 U/L
>6 wk–adult male	20–200 U/L	20–200 U/L
>6 wk–adult female	20–180 U/L	20–180 U/L

TABLE 27-1

## REFERENCE VALUES (Continued)

	Conventional Units	SI Units
<b>CREATININE (SERUM)<sup>2</sup> (Enzymatic)</b>		
Cord	0.6–1.2 mg/dL	53–106 $\mu$ mol/L
Newborn	0.3–1.0 mg/dL	27–88 $\mu$ mol/L
Infant	0.2–0.4 mg/dL	18–35 $\mu$ mol/L
Child	0.3–0.7 mg/dL	27–62 $\mu$ mol/L
Adolescent	0.5–1.0 mg/dL	44–88 $\mu$ mol/L
Adult male	0.9–1.3 mg/dL	80–115 $\mu$ mol/L
Adult female	0.6–1.1 mg/dL	53–97 $\mu$ mol/L
<b>ERYTHROCYTE SEDIMENTATION RATE (ESR)<sup>2</sup></b>		
Child	0–10 mm/hr	
Adult male	0–15 mm/hr	
Adult female	0–20 mm/hr	
<b>FERRITIN<sup>2</sup></b>		
Newborn	25–200 ng/mL	56–450 pmol/L
1 mo	200–600 ng/mL	450–1350 pmol/L
2–5 mo	50–200 ng/mL	112–450 pmol/L
6 mo–15 yr	7–140 ng/mL	16–315 pmol/L
Adult male	20–250 ng/mL	45–562 pmol/L
Adult female	10–120 ng/mL	22–270 pmol/L
<b>FIBRINOGEN</b>		
(See Chapter 14)		
<b>FOLATE (SERUM)<sup>3</sup></b>		
Newborn	16–72 ng/mL	16–72 nmol/L
Child	4–20 ng/mL	4–20 nmol/L
Adult	10–63 ng/mL	10–63 nmol/L
<b>FOLATE (RBC)<sup>2</sup></b>		
Newborn	150–200 ng/mL	340–453 nmol/L
Infant	74–995 ng/mL	168–2254 nmol/L
2–16 yr	>160 ng/mL	>362 nmol/L
>16 yr	140–628 ng/mL	317–1422 nmol/L
<b>GALACTOSE<sup>2</sup></b>		
Newborn	0–20 mg/dL	0–1.11 mmol/L
Older child	<5 mg/dL	<0.28 mmol/L
<b>GAMMA-GLUTAMYL TRANSFERASE (GGT)<sup>2,5</sup></b>		
(Major sources: Liver [biliary tree] and kidney)		
Cord	37–193 U/L	37–193 U/L
0–1 mo	13–147 U/L	13–147 U/L
1–2 mo	12–123 U/L	12–123 U/L
2–4 mo	8–90 U/L	8–90 U/L
4 mo–10 yr	5–32 U/L	5–32 U/L

Continued

**TABLE 27-1**

**REFERENCE VALUES (Continued)**

	Conventional Units	SI Units
<b>GAMMA-GLUTAMYL TRANSFERASE (GGT) (Continued)</b>		
10–15 yr	5–24 U/L	5–24 U/L
Adult male	11–49 U/L	11–49 U/L
Adult female	7–32 U/L	7–32 U/L
<b>GLUCOSE (SERUM)<sup>2,5</sup></b>		
Preterm	20–60 mg/dL	1.1–3.3 mmol/L
Newborn, <1 day	40–60 mg/dL	2.2–3.3 mmol/L
Newborn, >1 day	50–90 mg/dL	2.8–5.0 mmol/L
Child	60–100 mg/dL	3.3–5.5 mmol/L
>16 yr	70–105 mg/dL	3.9–5.8 mmol/L
<b>HAPTOGLOBIN<sup>2</sup></b>		
Newborn	5–48 mg/dL	50–480 mg/L
>30 days	26–185 mg/dL	260–1850 mg/L
<b>HEMOGLOBIN A<sub>1c</sub><sup>7</sup></b>		
Normal	4.5%–5.6%	
At risk for diabetes	5.7%–6.4%	
Diabetes mellitus	≥6.5%	
<b>HEMOGLOBIN F, % TOTAL HEMOGLOBIN (MEAN [SD])<sup>2</sup></b>		
1 day	77.0 (7.3)	
5 days	76.8 (5.8)	
3 wk	70.0 (7.3)	
6–9 wk	52.9 (11)	
3–4 mo	23.2 (16)	
6 mo	4.7 (2.2)	
8–11 mo	1.6 (1.0)	
Adult	<2.0	
<b>IRON<sup>2</sup></b>		
Newborn	100–250 mcg/dL	17.9–44.8 μmol/L
Infant	40–100 mcg/dL	7.2–17.9 μmol/L
Child	50–120 mcg/dL	9.0–21.5 μmol/L
Adult male	65–175 mcg/dL	11.6–31.3 μmol/L
Adult female	50–170 mcg/dL	9.0–30.4 μmol/L
<b>LACTATE<sup>2,3</sup></b>		
Capillary blood:		
0–90 days	9–32 mg/dL	1.1–3.5 mmol/L
3–24 mo	9–30 mg/dL	1.0–3.3 mmol/L
2–18 yr	9–22 mg/dL	1.0–2.4 mmol/L
Venous	4.5–19.8 mg/dL	0.5–2.2 mmol/L
Arterial	4.5–14.4 mg/dL	0.5–1.6 mmol/L
<b>LACTATE DEHYDROGENASE (AT 37°C)<sup>2</sup></b>		
(Major sources: Myocardium, liver, skeletal muscle, erythrocytes, platelets, and lymph nodes)		
0–4 days	290–775 U/L	290–775 U/L
4–10 days	545–2000 U/L	545–2000 U/L

TABLE 27-1

## REFERENCE VALUES (Continued)

	Conventional Units			SI Units				
LACTATE DEHYDROGENASE (Continued)								
10 days–24 mo	180–430 U/L			180–430 U/L				
24 mo–12 yr	110–295 U/L			110–295 U/L				
>12 yr	100–190 U/L			100–190 U/L				
LEAD <sup>2</sup>								
Child	<10 mcg/dL			<0.48 μmol/L				
LIPASE <sup>3</sup>								
0–30 days	6–55 U/L			6–55 U/L				
1–6 mo	4–29 U/L			4–29 U/L				
6–12 mo	4–23 U/L			4–23 U/L				
>1 yr	3–32 U/L			3–32 U/L				
	Cholesterol (mg/dL)			LDL (mg/dL)			HDL (mg/dL)	
	Desirable	Borderline	High	Optimal	Near/ Above optimal	Border- line	High	Desirable
LIPIDS <sup>8,9</sup>								
Child/ adoles- cent	<170	170–199	>200	<110		110–129	>130	>35
Adult	<200	200–239	<240	<100	100–129	130–159	>160	40–60
	Conventional Units			SI Units				
MAGNESIUM <sup>2</sup>	1.6–2.4 mg/dL			0.63–1.05 mmol/L				
METHEMOGLOBIN <sup>2</sup>	0.78% (±0.37%) of total hemoglobin							
OSMOLALITY <sup>2</sup>	275–295 mOsm/kg (neonates as low as 266)					275–295 mmol/kg		
PHENYLALANINE <sup>2</sup>								
Preterm	2.0–7.5 mg/dL			121–454 μmol/L				
Newborn	1.2–3.4 mg/dL			73–206 μmol/L				
Adult	0.8–1.8 mg/dL			48–109 μmol/L				
PHOSPHORUS <sup>2</sup>								
0–9 days	4.5–9.0 mg/dL			1.45–2.91 mmol/L				
10 days–24 mo	4–6.5 mg/dL			1.29–2.10 mmol/L				
3–9 yr	3.2–5.8 mg/dL			1.03–1.87 mmol/L				
10–15 yr	3.3–5.4 mg/dL			1.07–1.74 mmol/L				
>15 yr	2.4–4.4 mg/dL			0.78–1.42 mmol/L				
PORCELAIN <sup>10</sup>	9.0–24.11 mg/dL			9.0–28.13 mmol/L				
POTASSIUM <sup>2</sup>								
Preterm	3.0–6.0 mEq/L			3.0–6.0 mmol/L				
Newborn	3.7–5.9 mEq/L			3.7–5.9 mmol/L				
Infant	4.1–5.3 mEq/L			4.1–5.3 mmol/L				
Child	3.4–4.7 mEq/L			3.4–4.7 mmol/L				
Adult	3.5–5.1 mEq/L			3.5–5.1 mmol/L				

Continued

TABLE 27-1

## REFERENCE VALUES (Continued)

		Conventional Units		SI Units		
PREALBUMIN <sup>3</sup>						
Newborn		7–39 mg/dL				
1–6 mo		8–34 mg/dL				
6 mo–4 yr		12–36 mg/dL				
4–6 yr		12–30 mg/dL				
6–19 yr		12–42 mg/dL				
PROTEIN ELECTROPHORESIS (g/dL) <sup>2</sup>						
Age	Total Protein	Albumin	α-1	α-2	β	γ
Cord	4.8–8.0					
Premature	3.6–6.0					
Newborn	4.6–7.0					
0–15 day	4.4–7.6	3.0–3.9	0.1–0.3	0.3–0.6	0.4–0.6	0.7–1.4
15 day–1 yr	5.1–7.3	2.2–4.8	0.1–0.3	0.5–0.9	0.5–0.9	0.5–1.3
1–2 yr	5.6–7.5	3.6–5.2	0.1–0.4	0.5–1.2	0.5–1.1	0.5–1.7
3–16 yr	6.0–8.0	3.6–5.2	0.1–0.4	0.5–1.2	0.5–1.1	0.5–1.7
≥16 yr	6.0–8.3	3.9–5.1	0.2–0.4	0.4–0.8	0.5–1.0	0.6–1.2
		Conventional Units		SI Units		
PYRUVATE <sup>3</sup>		0.7–1.32 mg/dL		0.08–0.15 mmol/L		
RHEUMATOID FACTOR <sup>2</sup>		<30 U/mL				
SODIUM <sup>1</sup>						
<1 yr		130–145 mEq/L		130–145 mmol/L		
>1 yr		135–147 mEq/L		135–147 mmol/L		
TOTAL IRON-BINDING CAPACITY (TIBC) <sup>2</sup>						
Infant		100–400 mcg/dL		17.9–71.6 μmol/L		
Adult		250–425 mcg/dL		44.8–76.1 μmol/L		
TOTAL PROTEIN						
(See Proteins)						
TRANSAMINASE (SGOT)						
(See Aspartate aminotransferase [AST])						
TRANSAMINASE (SGPT)						
(See Alanine aminotransferase [ALT])						
TRANSFERRIN <sup>2</sup>						
Newborn		130–275 mg/dL		1.30–2.75 g/L		
3 mo–16 yr		203–360 mg/dL		2.03–3.6 g/L		
Adult		215–380 mg/dL		2.15–3.8 g/L		

TABLE 27-1

## REFERENCE VALUES (Continued)

TOTAL TRIGLYCERIDE <sup>3</sup>				
	Conventional Units (mg/dL)		SI Units (mmol/L)	
	Male	Female	Male	Female
0–7 days	21–182	28–166	0.24–2.06	0.32–1.88
8–30 days	30–184	30–165	0.34–2.08	0.34–1.86
31–90 days	40–175	35–282	0.45–1.98	0.4–3.19
91–180 days	45–291	50–355	0.51–3.29	0.57–4.01
181–365 days	45–501	36–431	0.51–5.66	0.41–4.87
1–3 yr	27–125	27–125	0.31–1.41	0.31–1.41
4–6 yr	32–116	32–116	0.36–1.31	0.36–1.31
7–9 yr	28–129	28–129	0.32–1.46	0.32–1.46
10–19 yr	24–145	37–140	0.27–1.64	0.42–1.58

	Conventional Units	SI Units
TROPONIN-I <sup>3</sup>		
0–30 days	<4.8 mcg/L	
31–90 days	<0.4 mcg/L	
3–6 mo	<0.3 mcg/L	
7–12 mo	<0.2 mcg/L	
1–18 yr	<0.1 mcg/L	
UREA NITROGEN <sup>1,2</sup>		
Premature (<1 wk)	3–25 mg/dL	1.1–8.9 mmol/L
Newborn	2–19 mg/dL	0.7–6.7 mmol/L
Infant/child	5–18 mg/dL	1.8–6.4 mmol/L
Adult	6–20 mg/dL	2.1–7.1 mmol/L
URIC ACID <sup>3,5</sup>		
0–30 days	1.0–4.6 mg/dL	0.059–0.271 mmol/L
1–12 mo	1.1–5.6 mg/dL	0.065–0.33 mmol/L
1–5 yr	1.7–5.8 mg/dL	0.1–0.35 mmol/L
6–11 yr	2.2–6.6 mg/dL	0.13–0.39 mmol/L
Male 12–19 yr	3.0–7.7 mg/dL	0.18–0.46 mmol/L
Female 12–19 yr	2.7–5.7 mg/dL	0.16–0.34 mmol/L
VITAMIN A (RETINOL) <sup>2,3</sup>		
Preterm	13–46 mcg/dL	0.46–1.61 $\mu$ mol/L
Full term	18–50 mcg/dL	0.63–1.75 $\mu$ mol/L
1–6 yr	20–43 mcg/dL	0.7–1.5 $\mu$ mol/L
7–12 yr	20–49 mcg/dL	0.9–1.7 $\mu$ mol/L
13–19 yr	26–72 mcg/dL	0.9–2.5 $\mu$ mol/L
VITAMIN B <sub>1</sub> (THIAMINE) <sup>2</sup>		
	4.5–10.3 mcg/dL	106–242 $\mu$ mol/L
VITAMIN B <sub>2</sub> (RIBOFLAVIN)		
	4–24 mcg/dL	106–638 nmol/L
VITAMIN B <sub>12</sub> (COBALAMIN) <sup>2</sup>		
Newborn	160–1300 pg/mL	118–959 pmol/L
Child/adult	200–835 pg/mL	148–616 pmol/L

Continued

**TABLE 27-1**  
**REFERENCE VALUES (Continued)**

	Conventional Units	SI Units
<b>VITAMIN C (ASCORBIC ACID)<sup>2</sup></b>	0.4–2.0 mg/dL	23–114 µmol/L
<b>VITAMIN D<sub>3</sub> (1,25-DIHYDROXY-VITAMIN D)<sup>2</sup></b>	16–65 pg/mL	42–169 pmol/L
<b>VITAMIN E<sup>1,2,3</sup></b>		
Preterm	0.5–3.5 mg/L	1–8 µmol/L
Full term	1.0–3.5 mg/L	2–8 µmol/L
1–12 yr	3.0–9.0 mg/L	7–21 µmol/L
13–19 yr	6.0–10.0 mg/L	14–23 µmol/L
<b>ZINC<sup>2</sup></b>	70–120 mcg/dL	10.7–18.4 mmol/L

\*CREST: Calcinosis, Raynaud syndrome, Esophageal dysmotility, Sclerodactyly, Telangiectasia.

**II. EVALUATION OF BODY FLUIDS**

- A. Evaluation of Transudate versus Exudate (Table 27-2)**
- B. Evaluation of Cerebrospinal Fluid (Table 27-3)**
- C. Evaluation of Synovial Fluid (Table 27-4)**

**TABLE 27-2**  
**EVALUATION OF TRANSUDATE VS. EXUDATE (PLEURAL, PERICARDIAL, OR PERITONEAL FLUID)**

Measurement*	Transudate	Exudate†
Protein (g/dL)	<3.0	>3.0
Fluid/serum ratio	<0.5	≥0.5
LDH (IU)	<200	≥200
Fluid/serum ratio (isoenzymes not useful)	<0.6	≥0.6
WBCs‡	<10,000/µL	>10,000/µL
RBCs	<5000	>5000
Glucose	>40	<40
pH§	>7.2	<7.2

\*Always obtain serum for glucose, LDH, protein, amylase, etc.  
†All of the following criteria do not have to be met for consideration as an exudate.  
‡In peritoneal fluid, WBC count >800/µL suggests peritonitis.  
§Collect anaerobically in a heparinized syringe.

**NOTE:** Amylase >5000 U/mL or pleural fluid/serum ratio >1 suggests pancreatitis.  
LDH, Lactate dehydrogenase; RBCs, red blood cells; WBCs, white blood cells.  
Data from Nichols DG, Ackerman AD, Carcillo JA, et al. *Rogers Textbook of Pediatric Intensive Care*. 4th ed. Baltimore: Williams & Wilkins, 2008.

TABLE 27-3

## EVALUATION OF CEREBROSPINAL FLUID

Age <sup>4,11</sup>	WBC Count/ $\mu$ L (median)	95th Percentile
0–28 days	0–12* (3)	19
29–56 days	0–6* (2)	9
Child	0–7	

	Conventional Units	SI Units
<b>GLUCOSE<sup>4,12</sup></b>		
Preterm	24–63 mg/dL	1.3–3.5 mmol/L
Term	34–119 mg/dL	1.9–6.6 mmol/L
Child	40–80 mg/dL	2.2–4.4 mmol/L

<b>PROTEIN<sup>4,12,13</sup></b>		
Preterm	65–150 mg/dL	0.65–1.5 g/L
0–14 days	79 ( $\pm$ 23) mg/dL <sup>†</sup>	0.79 ( $\pm$ 0.23) g/L <sup>†</sup>
15–28 days	69 ( $\pm$ 20) mg/dL <sup>†</sup>	0.69 ( $\pm$ 0.20) g/L <sup>†</sup>
29–42 days	58 ( $\pm$ 17) mg/dL <sup>†</sup>	0.58 ( $\pm$ 0.17) g/L <sup>†</sup>
43–56 days	53 ( $\pm$ 17) mg/dL <sup>†</sup>	0.53 ( $\pm$ 0.17) g/L <sup>†</sup>
Child	5–40 mg/dL	5–40 mg/dL

**OPENING PRESSURE (LATERAL RECUMBENT POSITION<sup>4,14</sup>)**

Newborn	8–11 cm H <sub>2</sub> O
1–18 yr	11.5–28 cm H <sub>2</sub> O*
Respiratory variations	0.5–1 cm H <sub>2</sub> O

\*Up to 90th percentile.

<sup>†</sup>Mean ( $\pm$ SD).

WBC, White blood cell.



TABLE 27-4

## CHARACTERISTICS OF SYNOVIAL FLUID IN THE RHEUMATIC DISEASES

Group	Condition	Synovial Complement	Color/Clarity	Viscosity	Mucin Clot	WBC Count	PMN (%)	Miscellaneous Findings
Noninflammatory	Normal	N	Yellow Clear	↑↑	G	<200	<25	
	Traumatic arthritis	N	Xanthochromic Turbid	↑	F–G	<2000	<25	Debris
	Osteoarthritis	N	Yellow Clear	↑	F–G	1000	<25	
Inflammatory	Systemic lupus erythematosus	↓	Yellow Clear	N	N	5000	10	Lupus cells
	Rheumatic fever	N–↑	Yellow Cloudy	↓	F	5000	10–50	
	Juvenile rheumatoid arthritis	N–↓	Yellow Cloudy	↓	Poor	15,000–20,000	75	
	Reiter syndrome	↑	Yellow Opaque	↓	Poor	20,000	80	Reiter cells
Pyogenic	Tuberculous arthritis	N–↑	Yellow-white Cloudy	↓	Poor	25,000	50–60	Acid-fast bacteria
	Septic arthritis	↑	Serosanguineous Turbid	↓	Poor	50,000–300,000	>75	Low glucose, bacteria

F, Fair; G, good; H, high; N, normal; PMN, polymorphonuclear leukocyte; WBC, white blood cell; ↓, decreased; ↑, increased.

From Cassidy JT, Petty RE. *Textbook of Pediatric Rheumatology*. 5th ed. Philadelphia: WB Saunders, 2005.

### III. CONVERSION FORMULAS

#### A. Temperature

1. **To convert degrees Celsius to degrees Fahrenheit:**

$$([9/5] \times \text{Temperature}) + 32$$

2. **To convert degrees Fahrenheit to degrees Celsius:**

$$(\text{Temperature} - 32) \times (5/9)$$

#### B. Length and Weight

1. **Length:** To convert inches to centimeters, multiply by 2.54.

2. **Weight:** To convert pounds to kilograms, divide by 2.2.

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# Chapter 28

## Biostatistics and Evidence-Based Medicine

Kari Bjornard, MD, MPH

### I. WEBSITES

#### A. Evidence-Based Resources

Centre for Evidence Based Medicine: <http://www.cebm.net>

Cochrane Reviews: <http://www.thecochranelibrary.com/view/0/index.html>

JAMA evidence: [www.jamaevidence.com](http://www.jamaevidence.com)

Johns Hopkins University Welch Medical Library: Evidence Based

Medicine Resources: <http://www.welch.jhu.edu/internet/ebr.html>

National Guideline Clearing House: <http://guideline.gov/>

University of Washington Healthlinks: Evidence-Based Practice:

<http://libguides.hsl.washington.edu/ebp>

#### B. Statistics Resources and Software

BMJ Statistics at Square One:

<http://www.bmj.com/collections/statsbk/index.dtl>

EpiInfo: <http://www.cdc.gov/epiinfo/>

Open Epi: <http://www.OpenEpi.com/OE2.3/Menu/OpenEpiMenu.htm>

### II. EVIDENCE-BASED MEDICINE

*Evidence-based medicine* refers to the method of integrating individual clinical expertise with the best available evidence from systematic research. It typically involves the following framework<sup>1</sup>:

#### A. Formulate the clinical question:

1. **Describe the patient or problem**, deciding whether the evidence you seek is on therapy, diagnosis or screening, prognosis, etiology or causation, cost-effectiveness, or a qualitative study.
2. **Describe the intervention** under consideration.
3. **Compare the intervention** with an alternative or standard of care if applicable.
4. **Formulate a specific outcome** of interest.

#### B. Search for the evidence to answer that question:

1. **Define search terms** that fit the clinical question.
2. **Develop your search strategy** using PubMed or other primary search sources. National Guideline Clearing House is a public resource for evidence-based practice guidelines: <http://guideline.gov/>.
3. **Review your results** and apply methodological filters to target the right type of study.

### C. Critically appraise the evidence—decide whether the study findings are valid and whether they are important to your question:

#### 1. **Therapy:**

- Were patient groups randomized for treatment?
- Were groups comparable and treated equally aside from the allocated treatment?
- Were study subjects and investigators blinded?
- Were all patients entering the trial accounted for in the groups they were randomized to (intention to treat)?
- How large was the treatment effect (see Section III C. 5–7), and how precise was the estimate of the treatment effect?

#### 2. **Diagnosis:**

- Was the test compared with an independent blind reference (gold) standard of diagnosis?
- Was the test evaluated in an appropriate spectrum of patients?

#### 3. **Prognosis:**

- Were study patients defined early in their course and followed up over a sufficient time?
- How likely are these outcomes over a defined time period, and how precise are estimates of prognosis?

#### 4. **Guidelines for judging causality of an association between a variable and outcome<sup>3</sup>:**

- Is there a temporal relationship?
- What is the strength of association?
- Is there a dose/response relationship?
- Were the findings replicated?
- Is there biological plausibility?
- Are there alternative explanations?
- What happens with cessation of exposure?
- Is this explanation consistent with other knowledge?
- How specific is the association?

- For more comprehensive criteria or other types of studies**, use appropriate appraisal frameworks.<sup>1</sup>

#### D. **Apply the evidence to the clinical question:**

If the evidence is valid and important, integrate it with your clinical expertise. Decide whether patients in the study were similar to your individual patient and whether:

- Patient will benefit from the therapy** and accept its regimen and consequences
- Test is available, affordable, accurate, and precise**
- Study findings will impact what to tell or offer the patient**

## III. BIOSTATISTICS FOR MEDICAL LITERATURE

### A. **Statistical Tests:** Table 28-1

- Different statistics apply to test a hypothesis of whether observed differences are statistically significant:**

TABLE 28-1

SOME COMMONLY USED STATISTICAL TESTS<sup>2</sup>

Parametric Test	Nonparametric Test	Purpose of Test	Example
Two-sample (unpaired) <i>t</i> test	Mann-Whitney <i>U</i> test	Compares two independent samples	To compare girls' heights with boys' heights
One-sample (paired) <i>t</i> test	Wilcoxon matched pairs test	Compares two sets of observations on a single sample	To compare weight of infants before and after a feeding
One-way analysis of variance ( <i>F</i> test) using total sum of squares (ANOVA)	Kruskall-Wallis analysis of variance by ranks	Effectively, a generalization of the paired <i>t</i> or Wilcoxon matched pairs test where three or more sets of observations are made on a single sample	To determine whether plasma glucose level is higher 1 hour, 2 hours, or 3 hours after a meal
Two-way analysis of variance (ANOVA)	Two-way analysis of variance by ranks	As above, but tests the influence (and interaction) of two different covariates	In the above example, to determine whether the results differ in male and female subjects
$\chi^2$ test	Fisher's exact test	Tests the null hypothesis that the distribution of a discontinuous variable is the same in two (or more) independent samples	To assess whether male or female adolescents are more likely to smoke
Product moment correlation coefficient (Pearson's <i>r</i> )	Spearman's rank correlation coefficient ( <i>r<sub>s</sub></i> )	Assesses the strength of the straight-line association between two continuous variables	To assess whether and to what extent plasma HbA <sub>1c</sub> concentration is related to plasma triglyceride concentration in diabetic patients
Regression by least squares method	Nonparametric regression (various tests)	Describes the numerical relation between two quantitative variables, allowing one value to be predicted from the other	To see how peak expiratory flow rate varies with height
Multiple regression by least squares method	Nonparametric regression (various tests)	Describes the numerical relationship between a dependent variable and several predictor variables (covariates)	To determine whether and to what extent a person's age, body fat, and sodium intake determine his or her blood pressure

Modified from Greenhalgh T. How to read a paper. Statistics for the non-statistician. I: different types of data need different statistical tests. *BMJ*. 1997;315:364-366.

- a. *Parametric statistical tests* are more powerful and used when data follow a normal distribution. *Nonparametric tests* are used when a normal distribution cannot be assumed; they rank data rather than taking absolute differences into account.
  - b. *Paired tests* are performed on paired data—for example, when the same parameter or observation is measured twice on each study subject, often before and after an intervention. *Unpaired tests* compare values from independent samples.
  - c. A *two-tailed test* has to be performed whenever an intervention could potentially lead to either an increase or decrease of the parameter. When the difference can go in only one direction, a *one-tailed test* can be used, which has greater statistical power.
2. **Correlation and regression describe the degree of linear association between two quantitative variables**, but they do not imply causation
- a. *Correlation* measures the strength of association between two values, expressed by the *correlation coefficient*  $r$ , also termed *Pearson's correlation coefficient*.
  - b. As a next step of describing association, the *regression equation* constructs the optimal straight line illustrating the correlation and allows prediction of a (dependent) variable from a known (independent) variable. The method of *multiple regression* is used when there are multiple independent variables. Multiple regression accounts for influences of various factors on the outcome.
3.  **$\alpha$  (Alpha—significance level of statistical test):**
- a. Definition: Probability of finding a statistical association by chance alone when in reality there is no association (type I error).
  - b. The level of  $\alpha$  is typically set at  $\leq 0.05$  but can be set where a study determines, which allows interpretation with 95% certainty that a detected association is true.
  - c. The  $P$  value (probability of a difference occurring by chance) is complementary to  $\alpha$ . If  $P$  is less than the significance level (typically set at  $\leq 0.05$ ), the detected association is unlikely to be due to chance alone.
4. **Power (of a statistical test):**
- a.  $\beta$  (Beta) = probability of finding no statistical association when there truly is one (type II error)
  - b. Power =  $1 - \beta$  = probability of finding a statistical association when there truly is one
  - c. Power typically set at a minimum of 0.80, which allows interpretation with 80% certainty that a detected lack of association is true
5. **Sample size:** Number of subjects required in a study to detect a certain (expected) effect magnitude with a sufficiently high power and sufficiently low  $\alpha$ .
6. **Confidence interval (95%):** Describes the 95% certainty that the reported interval contains the true population value. When confidence intervals (CIs) for groups overlap, they do not differ in a statistically significant manner.

- 7. **Confounding:** Variable associated with both the disease and the exposure variable, which can cause a misperceived relationship between the disease and exposure. Can be controlled for by matching, blinding, and randomization.
- 8. **Effect modification (interaction):** Variable that affects or modifies the observed effect of a risk factor or exposure on disease status
  - a. Stratification can elucidate effect modification if there is a difference in the risk ratio across strata.

**B. Study Design Comparison (Table 28-2)**

TABLE 28-2			
STUDY DESIGN COMPARISON			
Design Type	Definition	Advantages	Disadvantages
Case-control (often called retrospective)	Define diseased subjects (cases) and non-diseased subjects (controls); compare proportion of cases with exposure (risk factor) with proportion of controls with exposure (risk factor)	Good for rare diseases Small sample size Shorter study times (not followed over time) Less expensive	Highest potential for biases (recall, selection, and others) Weak evidence for causality No prevalence, PPV, NPV
Cohort (usually prospective; occasionally retrospective)	In study population, define exposed group (with risk factor) and non-exposed group (without risk factor)  Over time, compare proportion of exposed group with outcome (disease) with proportion of non-exposed group with outcome (disease)	Defines incidence Stronger evidence for causality  Decreases biases (sampling, measurement, reporting)	Expensive Long study times May not be feasible for rare diseases/outcomes  Factors related to exposure and outcome may falsely alter effect of exposure on outcome (confounding)
Cross-sectional	In study population, concurrently measure outcome (disease) and risk factor  Compare proportion of diseased group with risk factor with proportion of non-diseased group with risk factor	Defines prevalence Short time to complete	Selection bias Weak evidence for causality

TABLE 28-2

## STUDY DESIGN COMPARISON (Continued)

Design Type	Definition	Advantages	Disadvantages
Clinical trial (experiment)	In study population, assign (randomly) subjects to receive treatment or receive no treatment Compare rate of outcome (e.g., disease cure) between treatment and nontreatment groups	Randomized blinded trial is gold standard Randomization reduces confounding Best evidence for causality	Expensive Risks of experimental treatments in humans Longer study time Not suitable for rare outcomes/diseases
Meta-analysis (type of systematic review)	Collates data from multiple independent studies to maximize precision and power in testing for statistical significance	Higher statistical power Can control for inter-study variation	Possible bias in exclusion of published studies or publication bias

NPV, Negative predictive value; PPV, positive predictive value.

### C. Measurements of Disease Occurrence and Treatment Effects (Table 28-3)

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#### 1. Prevalence:

- Proportion of study population who have a disease (at one point in time)
- Number of total cases in a population (old and new) at a specific time, divided by total population at that time
- Prevalence = incidence  $\times$  duration of disease
- In cross-sectional studies (see Table 28-3):

$$(A + B)/(A + B + C + D)$$

#### 2. Incidence:

- Number of new cases in study population who newly develop an outcome (disease) per total study population at risk per given time period
- Number of new cases divided by the total population over a given time period
- For cohort studies and clinical trials (see Table 28-3):

$$(A + B)/(A + B + C + D)$$

#### 3. Relative risk (RR):

- Ratio of incidence of disease among people with risk factor to incidence of disease among people without risk factor
- For cohort studies or clinical trials (see Table 28-3):

$$[A/(A + C)]/[B/(B + D)]$$

#### c. Values:

- RR = 1: No effect of exposure (or treatment) on outcome (or disease)
- RR < 1: Exposure or treatment protective against outcome
- RR > 1: Exposure or treatment increases probability of outcome



TABLE 28-3

## GRID FOR CALCULATIONS IN CLINICAL STUDIES

Disease or Outcome	Exposure or Risk Factor or Treatment	
	Positive	Negative
Positive	A	B
Negative	C	D

4. **Odds ratio (OR):**

- a. For case-control studies, ratio of [odds of having risk factor in people with disease (A/B)] to [odds of having risk factor in people without disease (C/D)] (see Table 28-3):

$$(A/B) / (C/D) = (A \times D) / (B \times C)$$

- b. OR approximates RR when disease is rare (incidence < 0.10):

- (1) OR = 1: No association between risk factor and disease
- (2) OR < 1: Suggests that risk factor is protective against disease
- (3) OR > 1: Suggests association between risk factor and disease

5. **Absolute risk reduction (ARR), absolute risk difference:**

- a. Definition: Absolute difference the treatment makes, expressed as difference between (risk of the outcome in control group) minus (risk of the outcome in treatment group)

6. **Relative risk reduction (RRR):**

- a. Definition: Clinical significance of treatment effect, expressed as (absolute risk reduction) divided by (risk of the outcome in control group), or  $1 - RR$

7. **Number needed to treat (NNT):**

- a. Definition: Number of patients to be treated with treatment under question to prevent one undesirable outcome expressed as the inverse of the ARR, or  $1 \div ARR$

**D. Measurements of Test Validity and Reliability (Table 28-4)**1. **Sensitivity (Sens):**

- a. Proportion of all diseased who have positive test (see Table 28-4):

$$A/(A + C)$$

- b. Measures the ability of the test to correctly identify those who have the disease. Use highly sensitive test to help exclude a disease. (Low false-negative rate. Desirable for screening tests.) Not affected by disease prevalence.

2. **Specificity (Spec):**

- a. Proportion of all non-diseased who have a negative test (see Table 28-4):

$$D/(B + D)$$

- b. Measures the ability of the test to correctly identify those who do not have the disease. Use highly specific test to help confirm a disease. (Low false-positive rate.) Not affected by disease prevalence.

TABLE 28-4

## GRID FOR EVALUATING A CLINICAL TEST

Test Result	Disease Status	
	Positive	Negative
Positive	A (true positive)	B (false positive)
Negative	C (false negative)	D (true negative)

3. **Positive predictive value (PPV):**

- a. Proportion of all those with positive tests who truly have disease (see Table 28-4):

$$A/(A + B)$$

- b. Increased PPV with higher disease prevalence and higher specificity (and to a lesser degree, higher sensitivity)

4. **Negative predictive value (NPV):**

- a. Proportion of all those with negative tests who truly do not have disease (see Table 28-4):

$$D/(C + D)$$

- b. Increased NPV with lower prevalence (rarer disease) and higher sensitivity

5. **Likelihood ratio (LR):**

- a. LR positive: Ability of positive test result to confirm diseased status:  
LR positive = (Sens)/(1 – Spec)

- b. LR negative: Ability of negative test result to confirm nondiseased status:

$$\text{LR negative} = (\text{Spec})/(1 - \text{Sens})$$

$$[\text{Alternative LR negative} = (1 - \text{Sens})/\text{Spec}]$$

- c. Good tests have LR  $\geq 10$ . (Good tests have LR  $\leq 0.1$  if using alternative LR-negative formula.) Physical examination findings often have LR of about 2.

- d. LR should not be affected by disease prevalence. Can be used to calculate increase in probability of disease from baseline prevalence with positive test (LR positive) and decrease in probability of disease from baseline prevalence with negative test (using alternative LR negative) for any level of disease prevalence.

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## PART IV

## FORMULARY



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# Chapter 29

## Drug Dosages

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Branden Engorn, MD; and Jamie Flerlage, MD*

### I. NOTE TO READER

The authors have made every attempt to check dosages and medical content for accuracy. Because of the incomplete data on pediatric dosing, many drug dosages will be modified after the publication of this text. We recommend that the reader check product information and published literature for changes in dosing, especially for newer medicines. The U.S. Food and Drug Administration (FDA) provides the following pediatric drug information data sources:

New Pediatric Labeling Information: [www.fda.gov/NewPedLabeling](http://www.fda.gov/NewPedLabeling)

Drug Safety Reporting Updates: [www.fda.gov/PedDrugSafety](http://www.fda.gov/PedDrugSafety)

Pediatric Study Characteristics Database: [www.fda.gov/PedStudies](http://www.fda.gov/PedStudies)

To prevent prescribing errors, the use of abbreviations has been greatly discouraged. The following is a list of abbreviations The Joint Commission considers prohibited for use.

THE JOINT COMMISSION

Official “Do Not Use” List\*

Do Not Use	Potential Problem	Use Instead
U (unit)	Mistaken for “0” (zero), the number “4” (four) or “cc”	Write “unit”
IU (International Unit)	Mistaken for IV (intravenous) or the number 10 (ten)	Write “International Unit”
Q.D., QD, q.d., qd (daily)	Mistaken for each other	Write “daily”
Q.O.D., QOD, q.o.d, qod (every other day)	Period after the Q mistaken for “l” and the “O” mistaken for “l”	Write “every other day”
Trailing zero (X.0 mg) <sup>†</sup>	Decimal point is missed	Write X mg
Lack of leading zero (.X mg)		Write 0.X mg
MS	Can mean morphine sulfate or magnesium sulfate	Write “morphine sulfate” Write “magnesium sulfate”
MSO <sub>4</sub> and MgSO <sub>4</sub>	Confused for one another	

\*Applies to all orders and all medication-related documentation that is handwritten (including free-text computer entry) or on preprinted forms.

<sup>†</sup>Exception: A “trailing zero” may be used only where required to demonstrate the level of precision of the value being reported, such as for laboratory results, imaging studies that report size of lesions, or catheter/tube sizes. It may not be used in medication orders or other medication-related documentation.

Additional Abbreviations, Acronyms, and Symbols (For possible future inclusion in the Official “Do Not Use” List)

Do Not Use	Potential Problem	Use Instead
> (greater than)	Misinterpreted as the number “7” (seven) or the letter “L”	Write “greater than”
< (less than)	Confused for one another	Write “less than”
Abbreviations for drug names	Misinterpreted due to similar abbreviations for multiple drugs	Write drug names in full
Apothecary units	Unfamiliar to many practitioners Confused with metric units	Use metric units
@	Mistaken for the number “2” (two)	Write “at”
cc	Mistaken for U (units) when poorly written	Write “mL” or “ml” or “milliliters” (“mL” is preferred)
µg	Mistaken for mg (milligrams), resulting in one thousand-fold overdose	Write “mcg” or “micrograms”

## II. SAMPLE ENTRY

**ACETAZOLAMIDE**

Diamox and generics

**Carbonic anhydrase inhibitor, diuretic**

Yes



Yes



1



C

**Tabs:** 125, 250 mg**Oral suspension:** 25 mg/mL **Capsules (extended release):** 500 mg**Injection (sodium):** 500 mg

Contains 2.05 mEq Na/500 mg drug

**Diuretic (PO, IV)****Child:** 5 mg/kg/dose once daily or every other day**Adult:** 250–375 mg/dose once daily or every other day**Glaucoma****Child:****PO:** 8–30 mg/kg/24 hr ÷ Q6–8 hr**IM/IV:** 20–40 mg/kg/24 hr ÷ Q6 hr; **max. dose:** 1000 mg/24 hr**Adult:****PO (simple chronic; open-angle):** 1000 mg/24 hr ÷ Q6 hr**IV (acute secondary; closed-angle):** For rapid decrease in intraocular pressure, administer 500 mg/dose IV**Seizures (extended-release product not recommended):****Child and adult:** 8–30 mg/kg/24 hr ÷ Q6–12 hr PO; **max. dose:** 1 g/24 hr**Urine alkalinization:****Adult:** 5 mg/kg/dose PO repeated BID–TID over 24 hr**Management of hydrocephalus (see remarks):** Start with 20 mg/kg/24 hr ÷ Q8 hr PO/IV; may increase to 100 mg/kg/24 hr up to a **max. dose** of 2 g/24 hr.**Pseudotumor cerebri (PO; see remarks):****Child:** Start with 25 mg/kg/24 hr ÷ once daily–QID; increase by 25 mg/kg/24 hr until clinical response or as tolerated up to a **maximum** of 100 mg/kg/24 hr.**Adolescent:** Start with 1 g/24 hr ÷ once daily–QID; increase by 250 mg/24 hr until clinical response or as tolerated up to a **maximum** of 4 g/24 hr.**Contraindicated** in hepatic failure, severe renal failure (GFR < 10 mL/min), and hypersensitivity to sulfonamides.**T<sub>1/2</sub>:** 2–6 hr; **do not use** sustained-release capsules in seizures; IM injection may be painful; bicarbonate replacement therapy may be required during long-term use (see *Citrate* or *Sodium Bicarbonate*). For use in pseudotumor cerebri, doses of 60 mg/kg/24 hr may be required.

Possible side effects (more likely with long-term therapy) include GI irritation, paresthesias, sedation, hypokalemia, acidosis, reduced urate secretion, aplastic anemia, polyuria, and development of renal calculi.

May increase toxicity of cyclosporine. Aspirin may increase toxicity of acetazolamide. May decrease the effects of salicylates, lithium, and phenobarbital. False-positive urinary protein may occur with several assays. **Adjust dose in renal failure (see Chapter 31).**



**III. EXPLANATION OF BREAST-FEEDING CATEGORIES**

See sample entry on p. 647.

- 1** Compatible
- 2** Use with caution
- 3** Unknown with concerns
- X** Contraindicated
- ?** Safety not established

**IV. EXPLANATION OF PREGNANCY CATEGORIES**

- A** Adequate studies in pregnant women have not demonstrated a risk to the fetus in the first trimester of pregnancy, and there is no evidence of risk in later trimesters.
- B** Animal studies have not demonstrated a risk to the fetus, but there are no adequate studies in pregnant women; or animal studies have shown an adverse effect, but adequate studies in pregnant women have not demonstrated a risk to the fetus during the first trimester of pregnancy, and there is no evidence of risk in later trimesters.
- C** Animal studies have shown an adverse effect on the fetus, but there are no adequate studies in humans; or there are no animal reproduction studies and no adequate studies in humans.
- D** There is evidence of human fetal risk, but the potential benefits from the use of the drug in pregnant women may be acceptable despite its potential risks.
- X** Studies in animals or humans demonstrate fetal abnormalities or adverse reaction; reports indicate evidence of fetal risk. The risk of use in pregnant women clearly outweighs any possible benefit.

**V. DRUG INDEX**

Trade Names	Generic Name
1,25-dihydroxycholecalciferol	Calcitriol
2-PAM*	Pralidoxime Chloride
3TC*	Lamivudine
5-aminosalicylic acid	Mesalamine
5-ASA	Mesalamine
5-FC*	Flucytosine
5-Fluorocytosine*	Flucytosine
8-Arginine Vasopressin*	Vasopressin
9-Fluorohydrocortisone*	Fludrocortisone Acetate
27% Elemental Ca	Calcium Chloride
A-200	Pyrethrins
Abelcet	Amphotericin B Lipid Complex
Absorica	Isotretinoin
Abstra	Fentanyl
Accolate	Zafirlukast
AccuNeb (prediluted nebulized solution)	Albuterol
Accutane	Isotretinoin
Acetadote	Acetylcysteine

\*Common abbreviation or other name (not recommended for use when writing a prescription).

Trade Names	Generic Name
Acticin	Permethrin
Actigall	Ursodiol
Actiq	Fentanyl
Activase	Alteplase
Acular, Acular LS	Ketorolac
Acuvail	Ketorolac
Aczone	Dapsone
Adalat CC	Nifedipine
Adderall, Adderall XR	Dextroamphetamine + Amphetamine
Adenocard	Adenosine
Adoxa	Doxycycline
Adrenaline	Epinephrine HCl
Advair Diskus, Advair HFA	Fluticasone Propionate and Salmeterol
Advil, Children's Advil	Ibuprofen
Aerospan	Flunisolide
Afrin	Oxymetazoline
AK-Poly-Bac Ophthalmic	Bacitracin + Polymyxin B
AK-Spore H.C. Otic	Polymyxin B Sulfate, Neomycin Sulfate, Hydrocortisone
AK-Sulf	Sulfacetamide Sodium Ophthalmic
AKTob	Tobramycin
AK-Tracin Ophthalmic	Bacitracin
Albuminar	Albumin, Human
Albutein	Albumin, Human
Aldactone	Spironolactone
Aleve [OTC]	Naproxen/Naproxen Sodium
Allegra, Allegra ODT	Fexofenadine
Allegra-D 12 Hour, Allegra-D 24 Hour	Fexofenadine + Pseudoephedrine
Allergen Ear Drops	Antipyrine and Benzocaine
Alloprim	Allopurinol
Almacone, Almacone II Double Strength	Aluminum Hydroxide with Magnesium Hydroxide
Alsuma	Sumatriptan Succinate
AlternagEL	Aluminum Hydroxide
Alu-Cap	Aluminum Hydroxide
Alvesco	Ciclesonide
AmBisome	Amphotericin B, Liposomal
Amicar	Aminocaproic Acid
Amikin	Amikacin Sulfate
Amnesteem	Isotretinoin
Amoclan	Amoxicillin-Clavulanic Acid
Amoxil	Amoxicillin
Amphadase	Hyaluronidase
Amphocin	Amphotericin B
Amphojel	Aluminum Hydroxide
Anacin	Aspirin
Anaprox	Naproxen/Naproxen Sodium
Ancef	Cefazolin
Ancobon	Flucytosine
Anectine	Succinylcholine
Antilirium	Physostigmine Salicylate

\*Common abbreviation or other name (not recommended for use when writing a prescription).

Trade Names	Generic Name
Antipyrine and Benzocaine Otic	Antipyrine and Benzocaine
Antizol	Fomepizole
Anzemet	Dolasetron
Apresoline	Hydralazine Hydrochloride
Apriso	Mesalamine
Aquachloral Suppettes	Chloral Hydrate
Aquasol A	Vitamin A
Aquasol E	Vitamin E
Aquavit-E	Vitamin E
Aralen	Chloroquine HCl/Phosphate
Aranesp	Darbepoetin Alfa
Arbinoxa	Carbinoxamine
Arestin	Minocycline
Aridol	Mannitol
Aristospan	Triamcinolone
ASA*	Aspirin
Asacol, Asacol HD	Mesalamine
Asmanex Twisthaler	Mometasone Furoate
Asprin Free Anacin	Acetaminophen
Astelin	Azelastine
Astepro	Azelastine
Astragraf XL	Tacrolimus
Ativan	Lorazepam
AtroPen	Atropine Sulfate
Atrovent	Ipratropium Bromide
Augmentin, Augmentin ES-600, Augmentin XR	Amoxicillin-Clavulanic Acid
Auralgan (available in Canada)	Antipyrine and Benzocaine
Auro Ear Drops	Carbamide Peroxide
Avinza	Morphine Sulfate
Avita	Tretinoin
Ayr Saline	Sodium Chloride—Inhaled Preparations
Azactam	Aztreonam
Azasan	Azathioprine
Azasite	Azithromycin
Azo-Standard [OTC]	Phenazopyridine HCl
Azulfidine, Azulfidine EN-Tabs	Sulfasalazine
Baciguent Topical	Bacitracin
Bactrim	Sulfamethoxazole and Trimethoprim
Bactroban, Bactroban Nasal	Mupirocin
BAL*	Dimercaprol
Beconase AQ	Beclomethasone Dipropionate
Benadryl	Diphenhydramine
Benzac AC Wash 2 ½, 5, 10; Benzac 5, 10	Benzoyl Peroxide
Beta-Val	Betamethasone
Bethkis	Tobramycin
Biaxin, Biaxin XL	Clarithromycin
Bicillin C-R, Bicillin C-R 900/300	Penicillin G Preparations—Penicillin G Benzathine and Penicillin G Procaine
Bicillin L-A	Penicillin G Preparations—Benzathine

\*Common abbreviation or other name (not recommended for use when writing a prescription).

Trade Names	Generic Name
Bio-Statín	Nystatin
Bioxiverz	Neostigmine
Bleph 10	Sulfacetamide Sodium Ophthalmic
Brevibloc	Esmolol HCl
Brexoxyl Creamy Wash	Benzoyl Peroxide
Brisdelle	Paroxetine
British anti-Lewisite	Dimercaprol
Bufferin	Aspirin
Bumex	Bumetanide
Buminate	Albumin, Human
Cafcit	Caffeine Citrate
Cafergot	Ergotamine Tartrate + Caffeine
Calcidol	Ergocalciferol
Caldolor	Ibuprofen
Calan, Calan SR	Verapamil
Calciferol	Ergocalciferol
Calcijex	Calcitriol
Calcionate	Calcium Glubionate
Calciqid	Calcium Glubionate
Cal-Citrate	Calcium Citrate
Calcium disodium versenate	Edetate (EDTA) Calcium Disodium
Cal-Glu	Calcium Gluconate
Cal-Lac	Calcium Lactate
Calphron	Calcium Acetate
Camphorated opium tincture	Paregoric
Canasa	Mesalamine
Cancidas	Caspofungin
Cankaid	Carbamide Peroxide
Capoten	Captopril
Carafate	Sucralfate
Carbatrol	Carbamazepine
Cardene, Cardene SR	Nicardipine
Cardizem, Cardizem SR, Cardizem CD, Cardizem LA	Diltiazem
Carnitor	Carnitine
Catapres, Catapres TTS	Clonidine
Cathflo Activase	Alteplase
Caysten	Aztreonam
Ceclor, Ceclor CD	Cefaclor
Cecon	Ascorbic Acid
Cedax	Ceftibuten
Cefotan	Cefotetan
Ceftin	Cefuroxime Axetil
Cefzil	Cefprozil
Celestone	Betamethasone
CellCept	Mycophenolate Mofetil
Cephulac	Lactulose
Ceptaz	Ceftazidime
Cerebyx	Fosphenytoin
Chemet	Succimer

\*Common abbreviation or other name (not recommended for use when writing a prescription).

Trade Names	Generic Name
Chloromycetin	Chloramphenicol
Chlor-Trimeton	Chlorpheniramine Maleate
Cholestyramine Light	Cholestyramine
Chronulac	Lactulose
Ciloxan ophthalmic	Ciprofloxacin
Cipro, Cipro XR, Ciprodex, Cipro HC Otic	Ciprofloxacin
Citracel	Calcium Citrate
Claforan	Cefotaxime
Claravis	Isotretinoin
Claritin, Claritin Children's Allergy, Claritin RediTabs	Loratadine
Claritin-D 12 Hour, Claritin-D 24 Hour	Loratadine + Pseudoephedrine
Cleocin-T, Cleocin	Clindamycin
Cogentin	Benzotropine Mesylate
Colace	Docusate
Colocort	Hydrocortisone
CoLyte	Polyethylene Glycol—Electrolyte Solution
Compazine	Prochlorperazine
Concerta	Methylphenidate HCl
Copegus	Ribavirin
Cordarone	Amiodarone HCl
Cordron-D NR, Cordron-D	Carbinoxamine + Pseudoephedrine
Coreg, Coreg CR	Carvedilol
Cortef	Hydrocortisone
Cortenema	Hydrocortisone
Cortifoam	Hydrocortisone
Cortisporin Otic	Polymyxin B Sulfate, Neomycin Sulfate, Hydrocortisone
Co-Trimoxazole	Sulfamethoxazole and Trimethoprim
Coumadin	Warfarin
Covera-HS	Verapamil
Cozaar	Losartan
Crolom	Cromolyn
Cruex	Clotrimazole
Cuprimine	Penicillamine
Curosurf	Surfactant, Pulmonary/Poractant Alfa
Cutivate	Fluticasone Propionate
Cuvposa	Glycopyrrolate
Cyanoject	Cyanocobalamin/Vitamin B <sub>12</sub>
Cyclogyl	Cyclopentolate
Cyclomydril	Cyclopentolate with Phenylephrine
Cyomin	Cyanocobalamin/Vitamin B <sub>12</sub>
Cytovene	Ganciclovir
D-3, D3-5, D3-50	Cholecalciferol
Dantrium	Dantrolene
Daraprim	Pyrimethamine
Daytrana	Methylphenidate HCl
DDAVP*	Desmopressin Acetate
DDS*	Dapsone
D Drops	Cholecalciferol
Debrox	Carbamide Peroxide

\*Common abbreviation or other name (not recommended for use when writing a prescription).

Trade Names	Generic Name
Decadron	Dexamethasone
Deltasone	Prednisone
Delzicol	Mesalamine
Deodorized tincture of opium	Opium Tincture
Depacon	Valproic Acid
Depakene	Valproic Acid
Depakote, Depakote ER	Divalproex Sodium
Depen	Penicillamine
Depo-Medrol	Methylprednisolone
Depo-Provera	Medroxyprogesterone
Depo-Sub Q Provera 104	Medroxyprogesterone
Desquam-E 5, Desquam-E 10	Benzoyl Peroxide
Desyrel (previously available as)	Trazodone
Dexedrine Spansules	Dextroamphetamine
DexFerrum	Iron—Injectable Preparations (iron dextran)
Dexpak Taperpak	Dexamethasone
DextroStat	Dextroamphetamine ± Amphetamine
Di-5-ASA*	Olsalazine
Dialume	Aluminum Hydroxide
Diaminodiphenylsulfone	Dapsone
Diamox	Acetazolamide
Diastat, Diastat AcuDial	Diazepam
Diflucan and others	Fluconazole
Digibind, DigiFab	Digoxin Immune Fab (Ovine)
Digitek	Digoxin
Dilacor XR	Diltiazem
Dilantin, Dilantin Infatab	Phenytoin
Dilaudid, Dilaudid-HP	Hydromorphone HCl
Di-mesalazine	Olsalazine
Dimetapp Children's Cold and Allergy	Brompheniramine with Phenylephrine
Diovan	Valsartan
Dipentum	Olsalazine
Diprolene, Diprolene AF	Betamethasone
Diprosone	Betamethasone
DisperMox	Amoxicillin
Ditropan, Ditropan XL	Oxybutynin Chloride
Diuril	Chlorothiazide
DMSA [dimercaptosuccinic acid]*	Succimer
Dobutrex (previously available as)	Dobutamine
Dolophine	Methadone HCl
Dopram	Doxapram HCl
Doryx	Doxycycline
Doxidan	Bisacodyl
Dramamine, Children's Dramamine	Dimenhydrinate
Drisdol	Ergocalciferol
Dulcolax	Bisacodyl
Dulera	Mometasone Furoate + Formoterol Fumarate
Duraclon	Clonidine
Duragesic	Fentanyl

\*Common abbreviation or other name (not recommended for use when writing a prescription).

<b>Trade Names</b>	<b>Generic Name</b>
Duramist 12-Hr Nasal	Oxymetazoline
Duricef	Cefadroxil
Dycill	Dicloxacillin Sodium
Dynacin	Minocycline
Dyrenium	Triamterene
EC-Naprosyn	Naproxen
Efidac/24-Pseudoephedrine	Pseudoephedrine
Elavil	Amitriptyline
Elidel	Pimecrolimus
Elimite	Permethrin
Eliphos	Calcium Acetate
Elitek	Rasburicase
Elixophyllin	Theophylline
Elocon	Mometasone Furoate
Emfamil D-Vi-Sol	Cholecalciferol
EMLA, Eutectic mixture of lidocaine and prilocaine	Lidocaine and Prilocaine
E-Mycin	Erythromycin Preparations
Enbrel	Etanercept
Endocet	Oxycodone and Acetaminophen
Endodan	Oxycodone and Aspirin
Enemeez	Docusate
Enlon	Edrophonium Chloride
Entocort EC	Budesonide
Enulose	Lactulose
Epaned	Enalapril Maleate
EpiPen	Epinephrine HCl
Epitol	Carbamazepine
Epivir, Epivir-HBV	Lamivudine
Epogen	Epoetin Alfa
Epsom salts	Magnesium Sulfate
Ergomar	Ergotamine Tartrate
Ery-Ped	Erythromycin
Erythrocin, Pediamycin, E-Mycin, Ery-Ped	Erythromycin
Erythropoietin	Epoetin Alfa
Eryzole	Erythromycin Ethylsuccinate and Acetylsulfisoxazole
Exalgo	Hydromorphone HCl
Extina	Ketoconazole
Famvir	Famciclovir
Fansidar	Pyrimethamine + Sulfadoxine
Felbatol	Felbamate
Fentora	Fentanyl
Feosol	Iron—Oral Preparations (Ferrous sulfate)
Fergon	Iron—Oral Preparations (Ferrous sulfate)
Fer-In-Sol	Iron—Oral Preparations (Ferrous gluconate)
Ferrlecit	Iron—Injectable Preparations (Ferric gluconate)
Feverall	Acetaminophen
Fiberall	Psyllium
First-Lansoprazole	Lansoprazole
First-Omeprazole	Omeprazole

\*Common abbreviation or other name (not recommended for use when writing a prescription).

Trade Names	Generic Name
FK506	Tacrolimus
Flagyl, Flagyl ER	Metronidazole
Flebogamma DIF	Immune Globulin
Fleet BabyLax	Glycerin
Fleet Laxative, Fleet Bisacodyl	Bisacodyl
Fleet Mineral Oil	Mineral Oil
Fleet, Fleet Phospho-Soda	Sodium Phosphate
Fletcher's Castoria	Senna/Sennosides
Flonase HFA	Fluticasone Propionate
Florinef Acetate	Fludrocortisone Acetate
Flovent Diskus	Fluticasone Propionate
Floxin, Floxin Otic	Ofloxacin
Flumadine	Rimantadine
Fluohydrisone	Fludrocortisone Acetate
Fluoritab	Fluoride
Focalin, Focalin XR	Dexmethylphenidate
Folvite	Folic Acid
Foradil Aerolizer	Formoterol
Fortamet	Metformin
Fortaz	Ceftazidime
Fortical Nasal Spray	Calcitonin—Salmon
Foscavir	Foscarnet
Fulvicin U/F, Fulvicin P/G	Griseofulvin
Fungizone	Amphotericin B
Furadantin	Nitrofurantoin
Gabitril	Tiagabine
Gablofen	Baclofen
Galzin	Zinc Salts, Systemic
Gamaplex	Immune Globulin
Gamma benzene hexachloride*	Lindane
Gammaked	Immune Globulin
Garamycin	Gentamicin
Gastrocrom	Cromolyn
Gas-X	Simethicone
Gengraf	Cyclosporine Modified
GlucaGen, Glucagon Emergency Kit	Glucagon HCl
Glucophage, Glucophage XR	Metformin
Gly-Oxide	Carbamide Peroxide
Glycate	Glycopyrrolate
GoLYTELY	Polyethylene Glycol—Electrolyte Solution
Gralise	Gabapentin
Granisol	Granisetron
Grifulvin V	Griseofulvin
Grisactin	Griseofulvin
Gris-PEG	Griseofulvin
Gyne-Lotrimin 3, Gyne-Lotrimin	Clotrimazole
H.P. Acthar Gel	Corticotropin
Haldol, Haldol Decanoate 50, Haldol Decanoate 100	Haloperidol
Hecoria	Tacrolimus

\*Common abbreviation or other name (not recommended for use when writing a prescription).



Trade Names	Generic Name
Hexadrol	Dexamethasone
Horizant	Gabapentin
Humatin	Paromomycin Sulfate
Hydro-Tussin CBX	Carbinoxamine + Pseudoephedrine
Hyalenex	Hyaluronidase
Hypersal	Sodium Chloride—Inhaled Preparations
Imitrex	Sumatriptan Succinate
Imodium, Imodium AD	Loperamide
Imuran	Azathioprine
Inapsine	Droperidol
Inderal, Inderal LA	Propranolol
Indocin, Indocin SR, Indocin IV	Indomethacin
Infasurf	Surfactant, Pulmonary/Calfactant
INFeD	Iron—Injectable Preparations (iron dextran)
INH*	Isoniazid
Intal (previously available as)	Cromolyn
Intropin (previously available as)	Dopamine
Intuniv	Guanfacine
Invanz	Ertapenem
Iosat	Potassium Iodide
Iquix	Levofloxacin
IsonaRif	Isoniazid
Isoptin SR	Verapamil
Isopto Carpine	Pilocarpine HCl
Isopto Hyoscine	Scopolamine Hydrobromide
Isuprel	Isoproterenol
Jantoven	Warfarin
Kadian	Morphine Sulfate
Kantrex	Kanamycin
Kaopectate	Bismuth Subsalicylate
Kao-Tin	Bismuth Subsalicylate
Kapvay	Clonidine
Kayexalate	Sodium Polystyrene Sulfonate
Keflex	Cephalexin
Kemstro	Baclofen
Kenalog	Triamcinolone
Keppra, Keppra XR	Levetiracetam
Ketalar	Ketamine
Kionex	Sodium Polystyrene Sulfonate
Klonopin	Clonazepam
Klout	Pyrethrins with Piperonyl Butoxide
Kondremul	Mineral Oil
Konsyl	Psyllium
K-PHOS Neutral	Phosphorus Supplements
Kristalose	Lactulose
Kytril	Granisetron
Lamictal, Lamictal ODT, Lamictal XR	Lamotrigine
Laniazid	Isoniazid
Lanoxin	Digoxin

\*Common abbreviation or other name (not recommended for use when writing a prescription).

Trade Names	Generic Name
Lariam	Mefloquine HCl
Lasix	Furosemide
Lax-Pills	Senna/Sennosides
Lazanda	Fentanyl
L-Carnitine	Carnitine
Levaquin, Quixin, Iquix	Levofloxacin
Levocarnitine	Carnitine
Levophed and others	Norepinephrine Bitartrate
Lialda	Mesalamine
Licide	Pyrethrins with Piperonyl Butoxide
Lidoderm	Lidocaine
Lioresal	Baclofen
Liquid Pred	Prednisone
Lithobid	Lithium
L-M-X	Lidocaine
Loniten (previously available as)	Minoxidil
Lopressor, Toprol-XL	Metoprolol
Lotrimin AF	Clotrimazole
Lotrimin AF	Miconazole
Lovenox	Enoxaparin
Luminal	Phenobarbital
Luride	Fluoride
Luvox CR	Fluvoxamine
Maalox, Maalox Maximum Strength Liquid	Aluminum Hydroxide with Magnesium Hydroxide
Macrobid	Nitrofurantoin
Macrodantin	Nitrofurantoin
Mag-200, Mag-Ox 400, Uro-Mag	Magnesium Oxide
Marinol	Dronabinol
Maxidex	Dexamethasone
Maxipime	Cefepime
Maxivate	Betamethasone
Maxolon	Metoclopramide
Medrol, Medrol Dosepack	Methylprednisolone
Mefoxin	Cefoxitin
Mephyton	Phytonadione/Vitamin K <sub>1</sub>
Mepron	Atovaquone
Merrem	Meropenem
Mestinon	Pyridostigmine Bromide
Metadate ER	Methylphenidate HCl
Metamucil	Psyllium
Methadose	Methadone HCl
Methylin, Methylin ER	Methylphenidate HCl
Metozolv	Metoclopramide
MetroCream	Metronidazole
MetroGel, MetroGel-Vaginal	Metronidazole
MetroLotion	Metronidazole
Miacalcin, Miacalcin Nasal Spray	Calcitonin—Salmon
Micatin	Miconazole
Microzide	Hydrochlorothiazide

\*Common abbreviation or other name (not recommended for use when writing a prescription).

Trade Names	Generic Name
Milk of Magnesia	Magnesium Hydroxide
Millipred	Prednisolone
Minocin	Minocycline
Mintezol	Thiabendazole
Mintox	Aluminum Hydroxide with Magnesium Hydroxide
MiraLax	Polyethylene Glycol—Electrolyte Solution
Monistat	Miconazole
Motrin, Children's Motrin	Ibuprofen
MS Contin	Morphine Sulfate
Mucomyst	Acetylcysteine
Mucosol	Acetylcysteine
Murine Ear	Carbamide Peroxide
Myambutol	Ethambutol HCl
Mycamine	Micafungin Sodium
Mycelex, Mycelex-7	Clotrimazole
Mycobutin	Rifabutin
Mycostatin	Nystatin
Myfortic	Mycophenolate Sodium
Mylanta Gas	Simethicone
Mylanta, Mylanta Extra Strength	Aluminum Hydroxide with Magnesium Hydroxide
Mylicon	Simethicone
Myorisan	Isotretinoin
Mysoline	Primidone
Nallpen	Nafcillin
Naprelan	Naproxen/Naproxen Sodium
Naprosyn, Naprosen DR	Naproxen/Naproxen Sodium
Narcan	Naloxone
Nasacort AQ	Triamcinolone
Nasalcrom	Cromolyn
Nasarel	Flunisolide
Nascobal	Cyanocobalamin/Vitamin B <sub>12</sub>
Nasonex	Mometasone Furoate
Nebcin	Tobramycin
NebuPent	Pentamidine Isethionate
Nembutal	Pentobarbital
NeoBenz Micro	Benzoyl Peroxide
Neo-fradin	Neomycin Sulfate
Neo-Polycin	Neomycin/Polymyxin B/Bacitracin
NeoProfen (IV)	Ibuprofen
Neoral	Cyclosporine
Neosporin, Neosporin Ophthalmic, Neo To Go	Neomycin/Polymyxin B/Bacitracin
Neosporin GU Irrigant	Neomycin/Polymyxin B
Neo-Synephrine	Phenylephrine HCl
Neo-Synephrine 12-Hr Nasal	Oxymetazoline
Nephron	Epinephrine, Racemic
Neupogen, G-CSF	Filgrastim
Neurontin	Gabapentin
Neut	Sodium Bicarbonate
Nexiclon XR	Clonidine

\*Common abbreviation or other name (not recommended for use when writing a prescription).

Trade Names	Generic Name
Nexium	Esomeprazole
Nexterone	Amiodarone HCl
Niacor	Niacin (Vitamin B <sub>3</sub> )
Niaspan	Niacin (Vitamin B <sub>3</sub> )
Nicotinic acid	Niacin (Vitamin B <sub>3</sub> )
Nifediac CC	Nifedipine
Niferex	Iron—Oral Preparations
Nilstat	Nystatin
Nipride (previously available as)	Nitroprusside
Nitro-Bid	Nitroglycerin
Nitro-Dur	Nitroglycerin
Nitro-Mist	Nitroglycerin
Nitropress	Nitroprusside
Nitrostat	Nitroglycerin
Nitro-Time	Nitroglycerin
Nix	Permethrin
Nizoral, Nizoral A-D	Ketoconazole
Noriate	Metronidazole
Normal Serum Albumin (Human)	Albumin, Human
Normodyne	Labetalol
Noroxin	Norfloxacin
Norvasc	Amlodipine
Nostrilla	Oxymetazoline
NuCort	Hydrocortisone
NuLYTELY	Polyethylene Glycol—Electrolyte Solution
Nutr-E-Sol	Vitamin E/ $\alpha$ -Tocopherol
NVP*	Nevirapine
Nydrizid	Isoniazid
OCL*	Polyethylene Glycol—Electrolyte Solution
Ocean	Sodium Chloride—Inhaled Preparations
Ocuflox	Ofloxacin
Ocusulf-10	Sulfacetamide Sodium Ophthalmic
Omnaris	Ciclesonide
Ofirmev	Acetaminophen
Omeprazole and Syrspond SF Alka	Omeprazole
Omnicef	Cefdinir
Omnipaque 140, Omnipaque 180, Omnipaque 240, Omnipaque 300, and Omnipaque 350	Iohexol
Omnipen	Ampicillin
Onfi	Clobazam
Onmel	Itraconazole
Opticrom	Cromolyn
Optivar	Azelastine
Oralone	Corticosteroid
Oramorph SR	Morphine Sulfate
Orapred, Orapred ODT	Prednisolone
Oraqix	Lidocaine and Prilocaine
Orasone	Prednisone
OraVerse	Phentolamine Mesylate

\*Common abbreviation or other name (not recommended for use when writing a prescription).

Trade Names	Generic Name
Orazinc	Zinc Salts, Systemic
Os-Cal	Calcium Carbonate
Osmitol	Mannitol
OsmoPrep	Sodium Phosphate
Oxtellar	Oxcarbazepine
Oxy-5, Oxy-10	Benzoyl Peroxide
OxyContin	Oxycodone
Oxytrol	Oxybutynin Chloride
Pacerone	Amiodarone HCl
Palasbumin	Albumin, Human
Palgic	Carbinoxamine
Pamelor	Nortriptyline Hydrochloride
Pamix	Pyrantel Pamoate
Panadol	Acetaminophen
Paracetamol	Acetaminophen
Pataday	Olopatadine
Patanase	Olopatadine
Patanol	Olopatadine
Pathocil	Dicloxacillin Sodium
Paxil, Paxil CR	Paroxetine
Pediaflor	Fluoride
Pedia-Lax	Glycerin
Pediamycin	Erythromycin Preparations
Pediapred	Prednisolone
Pediazole	Erythromycin Ethylsuccinate and Acetylsulfisoxazole
PediOtic	Polymyxin B Sulfate, Neomycin Sulfate, Hydrocortisone
Pentam 300	Pentamidine Isethionate
Pentasa	Mesalamine
Pepcid, Pepcid AC [OTC], Maximum Strength Pepcid AC [OTC], Pepcid Complete [OTC], Pepcid RPD	Famotidine
Pepto-Bismol	Bismuth Subsalicylate
Percocet	Oxycodone and Acetaminophen
Percodan	Oxycodone and Aspirin
Perforomist	Formoterol
Periactin (previously available as)	Cyproheptadine
Periostat	Doxycycline
Pexeva	Paroxetine
Pfizerpen	Penicillin G Preparations—Aqueous Potassium and Sodium
PGE <sub>1</sub> *	Alprostadil
Phazyme	Simethicone
Phenergan	Promethazine
Phenytek	Phenytoin
PhosLo	Calcium Acetate
Phoslyra	Calcium Acetate
Pilopine HS	Pilocarpine HCl
Pima	Potassium Iodide
Pin-Rid	Pyrantel Pamoate

\*Common abbreviation or other name (not recommended for use when writing a prescription).

Trade Names	Generic Name
Pin-X	Pyrantel Pamoate
Pipracil	Piperacillin
Pitressin	Vasopressin
Plaquenil	Hydroxychloroquine
Polymox	Amoxicillin
Polysporin Ophthalmic	Bacitracin + Polymyxin B
Polysporin Topical	Bacitracin + Polymyxin B
Polytrim Ophthalmic Solution	Polymyxin B Sulfate and Trimethoprim Sulfate
Posture-D	Calcium Phosphate, Tribasic
Potassium Phosphate	Phosphorus Supplements
Precidex	Dexmedetomidine
Prelone	Prednisolone
Prevacid, Prevacid SoluTab	Lansoprazole
Prevalite	Cholestyramine
Prilosec, Prilosec OTC	Omeprazole
Primacor	Milrinone
Primaxin IV	Imipenem and Cilastatin
Principen	Ampicillin
Prinivil	Lisinopril
Privagen	Immune Globulin
ProAir HFA	Albuterol
Procanbid	Procainamide
Procardia, Procardia XL	Nifedipine
ProCentra	Dextroamphetamine Sulfate
Procrit	Epoetin Alfa
Proglycem	Diazoxide
Prograf	Tacrolimus
Pronestyl	Procainamide
Pronto	Pyrethrins
Prostaglandin E <sub>1</sub>	Alprostadil
Prostigmin	Neostigmine
Prostin VR Pediatric	Alprostadil
Protonix	Pantoprazole
Protopam	Pralidoxime Chloride
Protopic	Tacrolimus
Protostat	Metronidazole
Proventil, Proventil HFA (aerosol inhaler)	Albuterol
Provera	Medroxyprogesterone
Prozac, Prozac Weekly	Fluoxetine Hydrochloride
Pseudo Carb Pediatric	Carbinoxamine + Pseudoephedrine
PTU*	Propylthiouracil
Pulmicort Respules, Pulmicort Flexhaler	Budesonide
Pulmozyme	Dornase Alfa/DNase
Pyrazinoic acid amide	Pyrazinamide
Pyridium	Phenazopyridine HCl
Pyrinyl	Pyrethrins
Qnasl	Beclomethasone Dipropionate
Quelicin, Quelicin-1000	Succinylcholine
Questran, Questran Light	Cholestyramine

\*Common abbreviation or other name (not recommended for use when writing a prescription).

Trade Names	Generic Name
Quinidex	Quinidine
Quixin	Levofloxacin
QVAR*	Beclomethasone Dipropionate
Raniclor	Cefaclor
Rapamune	Sirolimus
Rayos	Prednisone
Rebetol	Ribavirin
Reese's Pinworm	Pyrantel Pamoate
Regitine	Phentolamine Mesylate
Reglan	Metoclopramide
Regonal	Pyridostigmine Bromide
Renova	Tretinoin
Resectisol	Mannitol
Restasis	Cyclosporine, Cyclosporine Microemulsion, Cyclosporine Modified
Retin-A, Retin-A Micro	Tretinoin
Retrovir, AZT	Zidovudine
Revatio	Sildenafil
Reversol	Edrophonium Chloride
Revonto	Dantrolene
R-Gene 10	Arginine Chloride
Rhinaris	Sodium Chloride—Inhaled Preparations
Rhinocort Aqua Nasal Spray	Budesonide
Ribaspheres	Ribavirin
RID	Pyrethrins
Rifadin	Rifampin
Rifamate	Isoniazid + Rifampin
Rifater	Pyrazinamide + Isoniazid + Rifampin
Rimactane	Rifampin
Riomet	Metformin
Risperdal, Risperdal M-Tab, Risperdal Consta	Risperidone
Ritalin, Ritalin SR, Ritalin LA	Methylphenidate HCl
Robinul	Glycopyrrolate
Rocaltrol	Calcitriol
Rocephin	Ceftriaxone
Rogaine, Men's Rogaine Extra Strength	Minoxidil
Romazicon	Flumazenil
Rowasa, SfRowasa	Mesalamine
Roxanol	Morphine Sulfate
Roxicet	Oxycodone and Acetaminophen
Roxicodone	Oxycodone
Roxilox	Oxycodone and Acetaminophen
RuLox Plus	Aluminum Hydroxide with Magnesium Hydroxide
S-2 Inhalant	Epinephrine, Racemic
Sabril	Vigabatrin
Salagen	Pilocarpine HCl
Salicylazosulfapyridine	Sulfasalazine
Sal-Tropine	Atropine Sulfate
Sancuso	Granisetron

\*Common abbreviation or other name (not recommended for use when writing a prescription).

Trade Names	Generic Name
Sandimmune	Cyclosporine
Sandostatin, Sandostatin LAR Depot	Octreotide Acetate
Sani-Supp	Glycerin
Sarafem	Fluoxetine Hydrochloride
SAS*	Sulfasalazine
Scopace	Scopolamine Hydrobromide
Selsun and others	Selenium Sulfide
Senna-Gen	Senna/Sennosides
Senokot	Senna/Sennosides
Septra	Sulfamethoxazole and Trimethoprim
Serevent Diskus	Salmeterol
Sildec	Carbinoxamine + Pseudoephedrine
Silvadene	Silver Sulfadiazine
Simply Saline	Sodium Chloride—Inhaled Preparations
Singulair	Montelukast
Slo-Niacin	Niacin (Vitamin B <sub>3</sub> )
Slow FE	Iron—Oral Preparations
Sodium Phosphate	Phosphorus Supplements
Solodyn	Minocycline
Solu-cortef	Hydrocortisone
Solu-Medrol	Methylprednisolone
Soluspan	Betamethasone
Sporanox	Itraconazole
SPS*	Sodium Polystyrene Sulfonate
SSD Cream, SSD AF Cream	Silver Sulfadiazine
SSKI*	Potassium Iodide
Stadol	Butorphanol
Stavzor	Valproic Acid
Stimate	Desmopressin Acetate
Stomach Relief, Stomach Relief Max St, Stomach Relief Plus	Bismuth Subsalicylate
Strattera	Atomoxetine
Streptase	Streptokinase
Sublimaze	Fentanyl
Sudafed	Pseudoephedrine
Sulfatrim	Sulfamethoxazole and Trimethoprim
Sulfazine, Sulfazine EC	Sulfasalazine
Sunkist Vitamin C	Ascorbic Acid
Suprax	Cefixime
Surfak	Docusate
Surfaxin	Surfactant, Pulmonary/Lucinactant
Survanta	Surfactant, Pulmonary/Beractant
Symbicort	Budesonide and Formoterol
Symmetrel	Amantadine Hydrochloride
Synagis	Palivizumab
Synercid	Quinupristin and Dalfopristin
Synthroid	Levothyroxine T <sub>4</sub>
Tagamet, Tagamet HB [OTC]	Cimetidine
Tambacor	Flecainide Acetate

\*Common abbreviation or other name (not recommended for use when writing a prescription).



Trade Names	Generic Name
Tamiflu	Oseltamivir Phosphate
Tapazole	Methimazole
Tazicef	Ceftazidime
Tazidime	Ceftazidime
Tegretol, Tegretol-XR	Carbamazepine
Tempra	Acetaminophen
Tenex	Guanfacine
Tenormin	Atenolol
Tensilon	Edrophonium Chloride
Tetrahydrocannabinol	Dronabinol
THC*	Dronabinol
Theo-24	Theophylline
Theochron	Theophylline
Thera-Ear	Carbamide Peroxide
Therazene	Silver Sulfadiazine
Thorazine	Chlorpromazine
ThyroSave	Potassium Iodide
ThyroShield	Potassium Iodide
Tiazac	Diltiazem
Tigan	Trimethobenzamide HCl
Timentin	Ticarcillin and Clavulanate
Tinactin	Tolnaftate
Tirosint	Levothyroxine
Tisit	Pyrethrins
TMP-SMX*	Sulfamethoxazole and Trimethoprim
TOBI, TOBI Podhaler	Tobramycin
Tobrex	Tobramycin
Tofranil, Tofranil-PM	Imipramine
Topamax	Topiramate
Topiragen	Topiramate
Toprol-XL	Metoprolol
Totacillin	Ampicillin
tPA*	Alteplase
Trandate	Labetalol
Transderm Scop	Scopolamine Hydrobromide
Trianex	Corticosteroid
Triaz	Benzoyl Peroxide
Triderm	Corticosteroid
Trileptal	Oxcarbazepine
Trilisate and others	Choline Magnesium Trisalicylate
TriLyte	Polyethylene Glycol—Electrolyte Solution
Trimethoprim-Sulfamethoxazole	Sulfamethoxazole and Trimethoprim
Trimox	Amoxicillin
Trokenndi XR	Topiramate
Tums	Calcium Carbonate
Tylenol	Acetaminophen
Tylenol #1, #2, #3, #4	Codeine and Acetaminophen
Tylox	Oxycodone and Acetaminophen
Uceris	Budesonide

\*Common abbreviation or other name (not recommended for use when writing a prescription).

Trade Names	Generic Name
Unasyn	Ampicillin/Sulbactam
Unithroid, Unithroid Direct	Levothyroxine
Urecholine	Bethanechol Chloride
Uro-KP-Neutral	Phosphorus Supplements
Urolene Blue	Methylene Blue
Urso 250, Urso Forte	Ursodiol
Vagistat-3	Miconazole
Valcyte	Valganciclovir
Valium	Diazepam
Valtrex	Valacyclovir
Vancocin	Vancomycin
Vantin	Cefpodoxime Proxetil
VariZig	Varicella-Zoster Immune Globulin (Human)
Vasotec	Enalapril Maleate
Vasotec IV	Enalaprilat
Veetids	Penicillin V Potassium
Venofer	Iron—Injectable Preparations (iron sucrose)
Ventolin HFA	Albuterol
Veramyst	Fluticasone Propionate
Verelan, Verelan PM	Verapamil
Veripred	Prednisolone
Vermox	Mebendazole
Versed (previously available as)	Midazolam
VFEND	Voriconazole
Viagra	Sildenafil
Vibramycin	Doxycycline
Vimpat	Lacosamide
Viramune, Viramune XR	Nevirapine
Virazole	Ribavirin
Visicol	Sodium Phosphate
Visine LR	Oxymetazoline
Vistaril	Hydroxyzine
Vistide	Cidofovir
Vitamin B <sub>1</sub>	Thiamine
Vitamin B <sub>2</sub>	Riboflavin
Vitamin B <sub>12</sub>	Cyanocobalamin/Vitamin B <sub>12</sub>
Vitamin B <sub>3</sub>	Niacin/Vitamin B <sub>3</sub>
Vitamin B <sub>6</sub>	Pyridoxine
Vitamin C	Ascorbic Acid
Vitrase	Hyaluronidase
Vitrasert	Ganciclovir
VoSpire ER	Albuterol
Vyvanse	Lisdexamfetamine
VZIG	Varicella-Zoster Immune Globulin (Human)
WinRho-SDF	Rh <sub>0</sub> (D) Immune Globulin Intravenous (Human)
Wycillin	Penicillin G Preparations—Procaine
Wymox	Amoxicillin
Xolegel	Ketoconazole
Xopenex, Xopenex HFA	Levalbuterol

\*Common abbreviation or other name (not recommended for use when writing a prescription).

Trade Names	Generic Name
Xylocaine	Lidocaine
Zantac, Zantac 75 [OTC], Zantac 150 Maximum Strength [OTC]	Ranitidine HCl
Zarontin	Ethosuximide
Zaroxolyn	Metolazone
Zegerid	Omeprazole
Zemuron	Rocuronium
Zenatane	Isotretinoin
Zenzedi	Dextroamphetamine Sulfate
Zestril	Lisinopril
Zetonna	Ciclesonide
Zinacef	Cefuroxime
Zirgan	Ganciclovir
Zithromax, Zithromax TRI-PAK, Zithromax Z-PAK, Zmax	Azithromycin
Zoderm	Benzoyl Peroxide
Zofran	Ondansetron
Zolicef	Cefazolin
Zoloft	Sertraline HCl
Zonegran	Zonisamide
ZORprin	Aspirin
Zosyn	Piperacillin with Tazobactam
Zovirax	Acyclovir
Zyloprim	Allopurinol
Zyrtec, Children's Zyrtec	Cetirizine
Zyrtec-D 12 Hour	Cetirizine + Pseudoephedrine
Zyvox	Linezolid

\*Common abbreviation or other name (not recommended for use when writing a prescription).

**ACETAMINOPHEN**

Tylenol, Tempra, Panadol, Feverall, Aspirin-Free Anacin, Paracetamol, Ofirmev, and many others

**Analgesic, antipyretic**



Yes



Yes



1



B/C

**Tabs [OTC]:** 325, 500, 650 mg

**Chewable tabs [OTC]:** 80, 160 mg; some may contain phenylalanine

**Infant drops, solution/suspension [OTC]:** 80 mg/0.8 mL

**Child suspension/syrup [OTC]:** 160 mg/5 mL

**Oral liquid [OTC]:** 160, 166.7 mg/5 mL; may contain 7% alcohol

**Extra-strength:** 166.7 mg/5 mL

**Elixir [OTC]:** 160 mg/5 mL

**Caplet [OTC]:** 160, 500, 650 mg

**Extended-release caplet/gelcap [OTC]:** 650 mg

**Gelcap [OTC]:** 500 mg

**Capsules [OTC]:** 500 mg

**Dispersible tabs (Tylenol Children's Meltaways) [OTC]:** 80 mg

**Suppositories [OTC]:** 80, 120, 325, 650 mg

**Injection:**

**Ofirmev:** 10 mg/mL (100 mL)

**PO/PR:**

**Neonate:** 10–15 mg/kg/dose PO/PR Q6–8 hr. Some advocate loading doses of 20–25 mg/kg/dose for PO dosing or 30 mg/kg/dose for PR dosing.

**Pediatric:** 10–15 mg/kg/dose PO/PR Q4–6 hr; **max. dose:** 90 mg/kg/24 hr. For rectal dosing, some may advocate a 40–45 mg/kg/dose loading dose.

**Dosing by weight (preferred) or age (PO/PR Q4–6 hr):**

Weight (lb)	Weight (kg)	Age	Dosage (mg)
6–11	2.7–5	0–3 mo	40
12–17	5.1–7.7	4–11 mo	80
18–23	7.8–10.5	1–2 yr	120
24–35	10.6–15.9	2–3 yr	160
36–47	16–21.4	4–5 yr	240
48–59	21.5–26.8	6–8 yr	320
60–71	26.9–32.3	9–10 yr	400
72–95	32.4–43.2	11 yr	480

**Adult:** 325–650 mg/dose

**Max. dose:** 4 g/24 hr, 5 doses/24 hr

**IV:**

**Term neonate and infant < 1 yr:** Labeled dosing from the UK and pharmacokinetic studies recommend 7.5–15 mg/kg/dose Q6 hr IV up to a **maximum** of 60 mg/kg/24 hr (see *Pediatr Anesth*. 2009;19:329–337). A phase 3 study is currently in progress in children <2 yr of age. See [www.clinicaltrials.gov](http://www.clinicaltrials.gov) for updated information.

**Child (≥2–12 yr) and adolescent/adult < 50 kg:** 15 mg/kg/dose Q6 hr, OR 12.5 mg/kg/dose Q4 hr IV up to a **maximum** of 75 mg/kg/24 hr.

**Adolescent and adult (≥50 kg):** 1000 mg Q6 hr, OR 650 mg Q4 hr up to a **maximum** of 4000 mg/24 hr.

Does not possess anti-inflammatory activity. **Use with caution** in patients with known G6PD deficiency.

$T_{1/2}$ : 1–3 hr, 2–5 hr in neonates; metabolized in the liver; see Chapter 2 and acetylcysteine for management of overdose.

Some preparations contain alcohol (7%–10%) and/or phenylalanine; all suspensions should be shaken before use.

Continued  
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ACETAMINOPHEN *continued*

May decrease the activity of lamotrigine and increase the activity/toxicity of busulfan, warfarin, and zidovudine. Barbiturates, phenytoin, rifampin, and anticholinergic agents (e.g., scopolamine) may decrease the effect of acetaminophen. Increased risk for hepatotoxicity may occur with barbiturates, carbamazepine, phenytoin, carmustine (with high acetaminophen doses), and chronic alcohol use. **Adjust dose in renal failure (see Chapter 31).**

**FOR IV USE:** Administer dose undiluted over 15 min. Most common side effects with IV use include nausea, vomiting, constipation, pruritus, agitation, and atelectasis in children; and nausea, vomiting, headache, and insomnia in adults.

Pregnancy category “B” for PO and PR routes and “C” for IV route.

**ACETAZOLAMIDE**

Diamox and generics

**Carbonic anhydrase inhibitor, diuretic**



Yes



Yes




1



C

**Tabs:** 125, 250 mg

**Oral suspension:** 25 mg/mL 

**Capsules (extended release):** 500 mg

**Injection (sodium):** 500 mg

Contains 2.05 mEq Na/500 mg drug

**Diuretic (PO, IV)**

**Child:** 5 mg/kg/dose once daily or every other day

**Adult:** 250–375 mg/dose once daily or every other day

**Glaucoma**

**Child:**

**PO:** 8–30 mg/kg/24 hr ÷ Q6–8 hr

**IM/IV:** 20–40 mg/kg/24 hr ÷ Q6 hr; **max. dose:** 1000 mg/24 hr

**Adult:**

**PO (simple chronic; open-angle):** 1000 mg/24 hr ÷ Q6 hr

**IV (acute secondary; closed-angle):** For rapid decrease in intraocular pressure, administer 500 mg/dose IV

**Seizures (extended-release product not recommended):**

**Child and adult:** 8–30 mg/kg/24 hr ÷ Q6–12 hr PO; **max. dose:** 1 g/24 hr

**Urine alkalization:**

**Adult:** 5 mg/kg/dose PO repeated BID–TID over 24 hr

**Management of hydrocephalus (see remarks):** Start with 20 mg/kg/24 hr ÷ Q8 hr PO/IV; may increase to 100 mg/kg/24 hr up to a **max. dose** of 2 g/24 hr.

**Pseudotumor cerebri (PO; see remarks):**

**Child:** Start with 25 mg/kg/24 hr ÷ once daily–QID; increase by 25 mg/kg/24 hr until clinical response or as tolerated up to a **maximum** of 100 mg/kg/24 hr.

**Adolescent:** Start with 1 g/24 hr ÷ once daily–QID; increase by 250 mg/24 hr until clinical response or as tolerated up to a **maximum** of 4 g/24 hr.

**Contraindicated** in hepatic failure, severe renal failure (GFR < 10 mL/min), and hypersensitivity to sulfonamides.

$T_{1/2}$ : 2–6 hr; **do not use** sustained-release capsules in seizures; IM injection may be painful; bicarbonate replacement therapy may be required during long-term use (see *Citrate* or *Sodium Bicarbonate*). For use in pseudotumor cerebri, doses of 60 mg/kg/24 hr may be required.

Possible side effects (more likely with long-term therapy) include GI irritation, paresthesias, sedation, hypokalemia, acidosis, reduced urate secretion, aplastic anemia, polyuria, and development of renal calculi.



ACETAZOLAMIDE *continued*

May increase toxicity of cyclosporine. Aspirin may increase toxicity of acetazolamide. May decrease the effects of salicylates, lithium, and phenobarbital. False-positive urinary protein may occur with several assays. **Adjust dose in renal failure (see Chapter 31).**

**ACETYLCYSTEINE**

Mucomyst, Mucosol, Acetadote

**Mucolytic, antidote for acetaminophen toxicity**



Yes



No



?



B

**Solution inhalation or oral use:** 100 mg/mL (10%) (10, 30 mL) or 200 mg/mL (20%) (4, 10, 30 mL); contains EDTA

**Injectable (Acetadote):** 200 mg/mL (20%) (30 mL); contains EDTA 0.5 mg/mL

**Acetaminophen poisoning (see Chapter 2 for additional information):**

**PO:** 140 mg/kg  $\times$  1, followed by 70 mg/kg/dose Q4 hr for a total of 17 doses. Repeat dose if vomiting occurs within 1 hr of administration.

**IV:** 150 mg/kg  $\times$  1 diluted in D<sub>5</sub>W or D<sub>5</sub>W/½NS administered over 60 min, followed by 50 mg/kg diluted in D<sub>5</sub>W administered over 4 hr, then 100 mg/kg diluted in D<sub>5</sub>W administered over 16 hr. Recommended weight-based drug dilution volumes:



Weight (kg)	Volume of D <sub>5</sub> W or D <sub>5</sub> W/½NS for 150 mg/kg Loading Dose Administered Over 60 min	Volume of D <sub>5</sub> W for 50 mg/kg Second Dose Administered Over 4 hr	Volume of D <sub>5</sub> W for 100 mg/kg Third Dose Administered Over 16 hr
≤20	3 mL/kg	7 mL/kg	14 mL/kg
>20–<40	100 mL	250 mL	500 mL
≥40	200 mL	500 mL	1000 mL

**Nebulizer:**

**Infant:** 1–2 mL of 20% solution (diluted with equal volume of H<sub>2</sub>O, or sterile saline to equal 10%), or 2–4 mL of 10% solution; administer TID–QID

**Child:** 3–5 mL of 20% solution (diluted with equal volume of H<sub>2</sub>O, or sterile saline to equal 10%), or 6–10 mL of 10% solution; administer TID–QID

**Adolescent:** 5–10 mL of 10% or 20% solution; administer TID–QID

**Distal intestinal obstruction syndrome in cystic fibrosis:**

**Adolescent and adult:** 10 mL of 20% solution (diluted in a sweet drink) PO QID with 100 mL of 10% solution PR as an enema once daily–QID



**Use with caution** in asthma. For nebulized use, give inhaled bronchodilator 10–15 min before use and follow with postural drainage and/or suctioning after acetylcysteine administration. Prior hydration is essential for distal intestinal obstruction syndrome treatment.

May induce bronchospasm, stomatitis, drowsiness, rhinorrhea, nausea, vomiting, and hemoptysis. Anaphylactoid reactions have been reported with IV use.

For IV use, elimination  $T_{1/2}$  is longer in newborns (11 hr) than in adults (5.6 hr).  $T_{1/2}$  is increased by 80% in patients with severe liver damage (Child-Pugh score of 7–13) and biliary cirrhosis (Child-Pugh score of 5–7).

For oral administration, chilling the solution and mixing with carbonated beverages, orange juice, or sweet drinks may enhance palatability.

**ACTH**

See Corticotropin

**ACYCLOVIR**

Zovirax and generics

**Antiviral**

No



Yes



1



B

**Capsules:** 200 mg**Tabts:** 400, 800 mg**Oral suspension:** 200 mg/5 mL; may contain parabens**Ointment:** 5% (15, 30 g)**Cream:** 5% (2, 5 g)**Injection in powder (with sodium):** 500, 1000 mg**Injection in solution (with sodium):** 50 mg/mL

Contains 4.2 mEq Na/1 g drug

**IMMUNOCOMPETENT:****Neonatal (HSV and HSV encephalitis; birth–3 mo):**

&lt;35 wk postconceptional age: 40 mg/kg/24 hr ÷ Q12 hr IV × 14–21 days

≥35 wk postconceptional age: 60 mg/kg/24 hr ÷ Q8 hr IV × 14–21 days

**Oral therapy for HSV suppression and neurodevelopment after treatment with IV acyclovir for 14–21 days:** 300 mg/m<sup>2</sup>/dose Q8 hr PO × 6 mo**HSV encephalitis (duration of therapy: 14–21 days):****Birth–3 mo:** Use above IV dosage.**3 mo–12 yr:** 60 mg/kg/24 hr ÷ Q8 hr IV; some experts recommend 45 mg/kg/24 hr ÷ Q8 hr IV

≥12 yr: 30 mg/kg/24 hr ÷ Q8 hr IV

**Mucocutaneous HSV (including genital, ≥12 yr):****Initial infection:****IV:** 15 mg/kg/24 hr or 750 mg/m<sup>2</sup>/24 hr ÷ Q8 hr × 5–7 days**PO:** 1000–1200 mg/24 hr ÷ 3–5 doses per 24 hr × 7–10 days. For pediatric dosing, use 40–80 mg/kg/24 hr ÷ Q6–8 hr × 5–10 days (**max. pediatric dose:** 1000 mg/24 hr).**Recurrence (≥12 yr):****PO:** 1000 mg/24 hr ÷ 5 doses per 24 hr × 5 days, or 1600 mg/24 hr ÷ Q12 hr × 5 days, or 2400 mg/24 hr ÷ Q8 hr × 2 days**Chronic suppressive therapy (≥12 yr):****PO:** 800 mg/24 hr ÷ Q12 hr for up to 1 year**Zoster:****IV (all ages):** 30 mg/kg/24 hr or 1500 mg/m<sup>2</sup>/24 hr ÷ Q8 hr × 7–10 days**PO (≥12 yr):** 4000 mg/24 hr ÷ 5×/24 hr × 5–7 days**Varicella:****IV (≥2 yr):** 30 mg/kg/24 hr or 1500 mg/m<sup>2</sup>/24 hr ÷ Q8 hr × 7–10 days**PO (≥2 yr):** 80 mg/kg/24 hr ÷ QID × 5 days (begin treatment at earliest signs/symptoms); **max. dose:** 3200 mg/24 hr**Max. dose** of oral acyclovir in children = 80 mg/kg/24 hr.**IMMUNOCOMPROMISED:****HSV:****IV (all ages):** 750–1500 mg/m<sup>2</sup>/24 hr ÷ Q8 hr × 7–14 days**PO (≥2 yr):** 1000 mg/24 hr ÷ 3–5 times/24 hr × 7–14 days; **max. dose** for child: 80 mg/kg/24 hr**HSV prophylaxis:****IV (all ages):** 750 mg/m<sup>2</sup>/24 hr ÷ Q8 hr during risk period**PO (≥2 yr):** 600–1000 mg/24 hr ÷ 3–5 times/24 hr during risk period; **max. dose** for child: 80 mg/kg/24 hr**Varicella or zoster:****IV (all ages):** 1500 mg/m<sup>2</sup>/24 hr ÷ Q8 hr × 7–10 days

ACYCLOVIR *continued***PO (consider using valacyclovir or famciclovir for better absorption):****Infant and child:** 20 mg/kg/dose (**max.** 800 mg) Q6 hr  $\times$  7–10 days**Adolescent and adult:** 20 mg/kg/dose (**max.** 800 mg) 5 times daily  $\times$  7–10 days**Max. dose** of oral acyclovir in children = 80 mg/kg/24 hr.**TOPICAL:**Apply 0.5-inch ribbon of 5% ointment for 4-inch-square surface area 6 times a day  $\times$  7 days.

See most recent edition of the AAP *Red Book* for further details. **Use with caution** in patients with preexisting neurologic or **renal impairment (adjust dose; see Chapter 31)** or dehydration. Adequate hydration and slow (1 hr) IV administration are essential to prevent crystallization in renal tubules. **Do not use** topical product on the eye or for prevention of recurrent HSV infections. Oral absorption is unpredictable (15%–30%); consider using valacyclovir or famciclovir for better absorption. Use ideal body weight for obese patients when calculating dosages. Resistant strains of HSV and VZV have been reported in immunocompromised patients (e.g., advanced HIV infection).

Can cause renal impairment; has been infrequently associated with headache, vertigo, insomnia, encephalopathy, GI tract irritation, elevated liver function tests, rash, urticaria, arthralgia, fever, and adverse hematologic effects. Probenecid decreases acyclovir renal clearance. Acyclovir may increase the concentration of tenofovir and meperidine (and its metabolite [normeperidine]).

**ADDERALL**See Dextroamphetamine  $\pm$  Amphetamine**ADENOSINE**

Adenocard and generics

**Antiarrhythmic**

No



No



?



C

**Injection:** 3 mg/mL (2, 4 mL); preservative free**Supraventricular tachycardia:****Neonate:** 0.05 mg/kg by rapid IV push over 1–2 seconds; may increase dose by 0.05 mg/kg increments Q2 min to **max.** of 0.25 mg/kg.**Child:** 0.1–0.2 mg/kg (**initial max. dose:** 6 mg) by rapid IV push over 1–2 seconds; may increase dose by 0.05 mg/kg increments Q2 min to **max.** of 0.25 mg/kg (up to 12 mg), or until termination of SVT. **Max. subsequent single dose:** 12 mg.**Adolescent and adults  $\geq 50$  kg:** 6 mg rapid IV push over 1–2 seconds; if no response after 1–2 min, give 12 mg rapid IV push. May repeat a second 12-mg dose after 1–2 min if required. **Max. single dose:** 12 mg.

**Contraindicated** in 2nd- and 3rd-degree AV block or sick sinus syndrome unless pacemaker placed. **Use with caution** in combination with digoxin (enhanced depressant effects on SA and AV nodes). If necessary, doses may be administered IO.

Follow each dose with NS flush.  $T_{1/2}$ :  $<10$  seconds.

May precipitate bronchoconstriction, especially in asthmatics. Side effects include transient asystole, facial flushing, headache, shortness of breath, dyspnea, nausea, chest pain, and lightheadedness.

Carbamazepine and diprydamole may increase effects/toxicity of adenosine. Methylxanthines (e.g., caffeine, theophylline) may decrease effects of adenosine.





**ALBUMIN, HUMAN**

Albuminar, Albutein, Buminate, Plasbumin, Normal Serum  
Albumin (Human), and many others

**Blood product derivative, plasma volume expander**



No



No



?



C

**Injection:** 5% (50 mg/mL) (50, 100, 250, 500, mL); 25% (250 mg/mL) (20, 50, 100 mL); both concentrations contain 130–160 mEq Na/L

**Hypoalbuminemia:**

**Child:** 0.5–1 g/kg/dose IV over 30–120 min; repeat Q1–2 days PRN

**Adult:** 25 g/dose IV over 30–120 min; repeat Q1–2 days PRN

**Max. dose:** 2 g/kg/24 hr

**Hypovolemia:**

**Child:** 0.5–1 g/kg/dose IV rapid infusion; may repeat PRN; **max. dose:** 6 g/kg/24 hr

**Adult:** 25 g/dose IV rapid infusion; may repeat PRN; **max. dose:** 250 g/48 hr

**Contraindicated** in cases of CHF or severe anemia; rapid infusion may cause fluid overload; hypersensitivity reactions may occur; may cause rapid increase in serum sodium levels.

**Caution:** 25% concentration contraindicated in preterm infants owing to risk of IVH. For infusion, use 5-micron filter or larger. Both 5% and 25% products are isotonic but differ in oncotic effects. Dilutions of the 25% product should be made with D<sub>5</sub>W or NS; **avoid sterile water as a diluent.**

**ALBUTEROL**

Proventil, VoSpire ER (sustained-release tabs);  
ProAir HFA, Proventil HFA, Ventolin HFA (aerosol inhaler);  
AccuNeb (prediluted nebulized solution); and many others

**$\beta_2$ -Adrenergic agonist**



No



No



1



C

**Tabs:** 2, 4 mg

**Sustained-release tabs:** 4, 8 mg

**Oral solution:** 2 mg/5 mL (473 mL)

**Aerosol inhaler (HFA):** 90 mcg/actuation (60 actuations/inhaler) (8.5 g)

**Nebulization solution (dilution required):** 0.5% (5 mg/mL) (0.5, 20 mL)

**Prediluted nebulized solution:** 0.63 mg in 3 mL NS, 1.25 mg in 3 mL NS, and 2.5 mg in 3 mL NS (0.083%); some preparations may be preservative free.

**Inhalations (nonacute use; see remarks):**

**Aerosol (HFA):** 2 puffs (90 mcg) Q4–6 hr PRN

**Nebulization:**

<1 yr: 0.05–0.15 mg/kg/dose Q4–6 hr

1–5 yr: 1.25–2.5 mg/dose Q4–6 hr

5–12 yr: 2.5 mg/dose Q4–6 hr

>12 yr: 2.5–5 mg/dose Q4–8 hr

**For use in acute exacerbations, more aggressive dosing may be used.**

**Oral (discouraged [see remarks]):**

2–6 yr: 0.3 mg/kg/24 hr PO  $\div$  TID; **max. dose:** 12 mg/24 hr

6–12 yr: 6 mg/24 hr PO  $\div$  TID; **max. dose:** 24 mg/24 hr

>12 yr and adult: 2–4 mg/dose PO TID–QID; **max. dose:** 32 mg/24 hr

Inhaled doses may be given more frequently than indicated. In such cases, consider cardiac monitoring and monitoring of serum potassium (hypokalemia). Systemic effects are dose related. Please verify concentration of nebulization solution used.

ALBUTEROL *continued*

Safety and efficacy for the treatment of symptoms or bronchospasms associated with obstructive airway disease have not been demonstrated for children <4 yr of age (either dose studied was not optimal in this age or drug is not effective in this age group).

Use of oral dosage form is discouraged owing to increased side effects and decreased efficacy compared to inhaled formulations.

Possible side effects include tachycardia, palpitations, tremor, insomnia, nervousness, nausea, and headache.

Use of tube spacers or chambers may enhance efficacy of metered dose inhalers and have been proven to be just as effective and sometimes safer than nebulizers.

**ALLOPURINOL**

Zyloprim, Alloprim, and generics

***Uric acid–lowering agent, xanthine oxidase inhibitor***



Yes



Yes



1



C

**Tabs:** 100, 300 mg

**Oral suspension:** 20 mg/mL 

**Injection (Alloprim):** 500 mg

Contains  $\approx 1.45$  mEq Na/500 mg drug

**For use in tumor lysis syndrome, see Chapter 22.**

**Child:**

**Oral:** 10 mg/kg/24 hr PO  $\div$  BID–QID; **max. dose:** 800 mg/24 hr

**Injectable:** 200 mg/m<sup>2</sup>/24 hr IV  $\div$  Q6–12 hr; **max. dose:** 600 mg/24 hr

**Adult:**

**Oral:** 200–800 mg/24 hr PO  $\div$  BID–TID

**Injectable:** 200–400 mg/m<sup>2</sup>/24 hr IV  $\div$  Q6–12 hr; **max. dose:** 600 mg/24 hr

**Adjust dose in renal insufficiency (see Chapter 31).** Must maintain adequate urine output and alkaline urine.

**Drug interactions:** Increases serum theophylline level; may increase the incidence of rash with ampicillin and amoxicillin; increased risk of toxicity with azathioprine, didanosine, and mercaptopurine; increased risk of hypersensitivity reactions with ACE inhibitors and thiazide diuretics. Use with didanosine is **contraindicated** owing to increased risk for didanosine toxicity. Rhabdomyolysis has been reported with clarithromycin use.

Side effects include rash, neuritis, hepatotoxicity, GI disturbance, bone marrow suppression, and drowsiness.

IV dosage form is very alkaline and must be **diluted to a minimum concentration** of 6 mg/mL and infused over 30 min.

**ALPROSTADIL**

Prostin VR Pediatric, Prostaglandin E<sub>1</sub>, PGE<sub>1</sub>  
*Prostaglandin E<sub>1</sub>, vasodilator*



No



No



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X

**Injection:** 500 mcg/mL (1 mL); contains dehydrated alcohol

**Neonate:**

**Initial:** 0.05–0.1 mcg/kg/min. Advance to 0.2 mcg/kg/min if necessary.

**Maintenance:** When increase in PaO<sub>2</sub> is noted, decrease immediately to lowest effective dose.

Usual dosage range: 0.01–0.4 mcg/kg/min; doses above 0.4 mcg/kg/min not likely to produce additional benefit.

**To prepare infusion:** See inside front cover.

For palliation only. Continuous vital sign monitoring essential. May cause apnea (10%–12%, especially in those weighing <2 kg at birth), fever, seizures, flushing, bradycardia, hypotension, diarrhea, gastric outlet obstruction, and reversible cortical proliferation of long bones (with prolonged use). May decrease platelet aggregation.

**ALTEPLASE**

Activase, Cathflo Activase, tPA

*Thrombolytic agent, tissue plasminogen activator*



Yes



Yes



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C

**Injection:**

**Cathflo Activase:** 2 mg

**Activase:** 50 mg (29 million units), 100 mg (58 million units)

Contains L-arginine and polysorbate 80.

**Occluded IV catheter:**

**Aspiration method:** Use 1 mg/1 mL concentration as follows:

**Central venous line (dosage per lumen, treating one lumen at a time):**

**<30 kg:** Instill a volume equal to 110% of internal lumen volume of the catheter

**NOT exceeding 2 mg.**

**≥30 kg:** 2 mg each lumen.

**Subcutaneous port:** Instill a volume equal to 110% of internal lumen and line volume of the port **NOT exceeding 2 mg.**

Instill into catheter over 1–2 min and leave in place for 2 hr before attempting blood withdrawal. After 2 hr, attempts to withdraw blood may be made Q2 hr for 3 attempts. Dose may be repeated once in 24 hours using a longer catheter dwell time of 3–4 hr. After 3–4 hr (repeat dose), attempts to withdraw blood may be made Q2 hr for 3 attempts. **DO NOT** infuse into patient.

**Systemic thrombolytic therapy (use in consultation with a hematologist [see remarks]):** Dosage regimens ranging from lower dosages (0.01 mg/kg/hr) to higher dosages (0.1–0.6 mg/kg/hr) have been reported (*Chest*. 2008;133:887S–968S). The length of continuous infusion is variable; patients may respond to longer or shorter courses of therapy.

Current use in the pediatric population is limited. May cause bleeding, rash, and increase prothrombin time.

**THROMBOLYTIC USE:** History of stroke, transient ischemic attacks, other neurologic disease, and hypertension are **contraindications for adults** but considered **relative contraindications for children**. Monitor fibrinogen, thrombin clotting time, PT, and APTT when used as a thrombolytic. For systemic thrombosis therapy, efficacy has been reported at 40%–97%, with

ALTEPLASE *continued*

the risk for bleeding at 3%–27%. Poor efficacy in VTE in children has been recently reported. **Use with caution** in severe hepatic or renal dysfunction (systemic use only).

Newborns have reduced plasminogen levels ( $\approx 50\%$  of adult values) that decrease the thrombolytic effects of alteplase. Plasminogen supplementation may be necessary.

**ALUMINUM HYDROXIDE**

Amphojel, Alu-Cap, Dialume, AlternaGEL and various generics

**Antacid, phosphate binder**



No



Yes



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**Oral suspension [OTC]:** 320 mg/5 mL (473 mL)

**Oral tablet:** 300, 600 mg

**Oral capsule (Alu-Cap):** 400 mg

Each 5 mL suspension contains  $< 0.13$  mEq Na.

**Antacid:**

**Child:** 300–900 mg PO 1–3 hr PC and HS

**Adult:** 600–1200 mg PO 1–3 hr PC and HS; **max. dose:** 3600 mg/24 hr

**Prophylaxis against GI bleeding (mL volume dosages are based on the 320 mg/5 mL oral suspension concentration):**

**Neonate:** 1 mL/kg/dose PO Q4 hr PRN

**Infant:** 2–5 mL PO Q1–2 hr

**Child:** 5–15 mL PO Q1–2 hr

**Adult:** 30–60 mL PO Q1–2 hr

**Hyperphosphatemia (administer all doses between meals and titrate to normal serum phosphorus):**

**Child:** 50–150 mg/kg/24 hr  $\div$  Q4–6 hr PO

**Adult:** 300–600 mg TID–QID PO between meals and QHS

**Max. dose** (all ages): 3000 mg/24 hr

**Use with caution** in patients with renal failure and upper GI hemorrhage.

Interferes with absorption of several orally administered medications, including digoxin, ethambutol, indomethacin, isoniazid, naproxen, mycophenolate, tetracyclines, fluoroquinolones (e.g., ciprofloxacin), and iron. Generally, **do not** take oral medications within 1–2 hours of taking aluminum hydroxide dose unless specified.

May cause constipation, decreased bowel motility, encephalopathy, and phosphorus depletion.

**ALUMINUM HYDROXIDE WITH MAGNESIUM HYDROXIDE**

Maalox, Maalox Maximum Strength Liquid, Mylanta, Mylanta Extra Strength, Almacone, Almacone Double Strength, RuLox, and many others generics (see remarks)

**Antacid**



No



Yes



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**Chewable tabs [OTC]:**  $\text{Al}(\text{OH})_3$  and  $\text{Mg}(\text{OH})_2$

Almacone: 200 mg  $\text{Al}(\text{OH})_3$ , 200 mg  $\text{Mg}(\text{OH})_2$ , and 20 mg simethicone

**Oral suspension [OTC] (see remarks):**

Maalox, Mylanta, and Almacone: Each 5 mL contains 200 mg  $\text{Al}(\text{OH})_3$ , 200 mg  $\text{Mg}(\text{OH})_2$ , and 20 mg simethicone (150, 360, 720 mL).

RuLox: Each 5 mL contains 200 mg  $\text{Al}(\text{OH})_3$ , 200 mg  $\text{Mg}(\text{OH})_2$ , and 25 mg simethicone (355 mL).

Mylanta Extra Strength, Maalox Maximum Strength liquid, and Almacone Double Strength: Each 5 mL contains 400 mg  $\text{Al}(\text{OH})_3$ , 400 mg  $\text{Mg}(\text{OH})_2$ , and 40 mg simethicone (360, 480 mL).

*Continued*

ALUMINUM HYDROXIDE WITH MAGNESIUM HYDROXIDE *continued*

**Mylanta Ultimate Strength:** Each 5 mL contains 500 mg AlOH, 500 mg MgOH (360 mL)

Many other combinations exist.

Contains 0.03–0.06 mEq Na/5 mL

Same as for aluminum hydroxide preparations. **Do not use** combination product for hyperphosphatemia.



May have laxative effect. May cause hypokalemia. **Use with caution** in patients with renal insufficiency (magnesium), gastric outlet obstruction.



Interferes with absorption of benzodiazepines, chloroquine, digoxin, naproxen, mycophenolate, phenytoin, quinolones (e.g., ciprofloxacin), tetracyclines, and iron. Generally, **do not take** oral medications within 1–2 hr of taking antacid dose unless specified.

**DO NOT use** Maalox Total Relief (bismuth subsalicylate), Mylanta Supreme Liquid (calcium carbonate + magnesium hydroxide), Maalox Regular Strength Chewable Tablets and Children's Mylanta Chewable Tablets (calcium carbonate), Maalox Maximum Strength Chewable (calcium carbonate and simethicone), Mylanta Gas (simethicone); these products do not contain aluminum hydroxide and magnesium hydroxide.

**AMANTADINE HYDROCHLORIDE**

Symmetrel and others

**Antiviral agent**



Yes



Yes



3



C

**Capsule:** 100 mg

**Tab:** 100 mg

**Oral solution or syrup:** 50 mg/5 mL (480 mL); may contain parabens

**Influenza A prophylaxis and treatment (for treatment, it is best to initiate therapy immediately after symptom onset, within 2 days [see remarks]):**



**1–9 yr:** 5 mg/kg/24 hr PO ÷ BID; **max. dose:** 150 mg/24 hr

**>9 yr:**

**<40 kg:** 5 mg/kg/24 hr PO ÷ BID; **max. dose** 200 mg/24 hr

**≥40 kg:** 200 mg/24 hr ÷ BID

**Alternative dosing for influenza A prophylaxis:**

**Child >20 kg and adult:** 100 mg/24 hr PO ÷ BID

**Prophylaxis (duration of therapy):**

**Single exposure:** At least 10 days

**Repeated/uncontrolled exposure:** Up to 90 days

Use with influenza A vaccine when possible.

**Symptomatic treatment (duration of therapy):**

Continue for 24–48 hr after disappearance of symptoms.

**Do not use** in first trimester of pregnancy. **Use with caution** in patients with liver disease, seizures, renal disease, CHF, peripheral edema, orthostatic hypotension, history of recurrent eczematoid rash, and in those receiving CNS stimulants. **Adjust dose in patients with renal insufficiency (see Chapter 31).**



CDC has reported resistance to influenza A and recommendations against use for treatment and prophylaxis. Check with local microbiology laboratories and CDC for seasonal susceptibility/resistance. Individuals immunized with live attenuated influenza vaccine should not receive amantadine prophylaxis for 14 days after the vaccine.

May cause dizziness, anxiety, depression, mental status change, rash (livedo reticularis), nausea, orthostatic hypotension, edema, CHF, and urinary retention. Impulse control disorder has been reported. Neuroleptic malignant syndrome has been reported with abrupt dose reduction or discontinuation (especially if patient is receiving neuroleptics).

**AMIKACIN SULFATE**

Amikin and many generics

**Antibiotic, aminoglycoside**

No



Yes



1



D

**Injection:** 250 mg/mL; may contain sodium bisulfite

Initial empirical dosage; patient specific dosage defined by therapeutic drug monitoring (see remarks).

**Neonates:** See the following table.

Postconceptional Age (wk)	Postnatal Age (days)	Dose (mg/kg/dose)	Interval (hr)
≤29*	0–7	18	48
	8–28	15	36
	>28	15	24
30–33	0–7	18	36
	>7	15	24
34–37	0–7	15	24
	>7	15	18–24†
≥38	0–7	15	24
	>7	15	12–18

\*Or significant asphyxia, PDA, indomethacin use, poor cardiac output, reduced renal function.

†Use Q36 hr interval for HIE patients receiving whole-body therapeutic cooling.

**Infant and child:** 15–22.5 mg/kg/24 hr ÷ Q8 hr IV/IM; infants and patients requiring higher doses (e.g., cystic fibrosis) may receive initial doses of 30 mg/kg/24 hr ÷ Q8 hr IV/IM**Cystic fibrosis (if available, use patient's previous therapeutic mg/kg dosage):****Conventional Q8 hr dosing:** 30 mg/kg/24 hr ÷ Q8 hr IV**High-dose extended interval (once daily) dosing (limited data):** 30–35 mg/kg/24 hr Q24 hr IV**Adult:** 15 mg/kg/24 hr ÷ Q8–12 hr IV/IM**Initial max. dose:** 1.5 g/24 hr, then monitor levels

Use with **caution** in preexisting renal, vestibular, or auditory impairment; concomitant anesthesia or neuromuscular blockers; neurotoxic, concomitant neurotoxic, ototoxic, or nephrotoxic drugs; sulfite sensitivity; and dehydration. **Adjust dose in renal failure (see Chapter 31).** Longer dosing intervals may be necessary for neonates receiving indomethacin for PDAs and for all patients with poor cardiac output. Rapidly eliminated in patients with cystic fibrosis, burns, and in febrile neutropenic patients. CNS penetration is poor beyond early infancy.



Therapeutic levels (using conventional dosing): Peak, 20–30 mg/L; trough 5–10 mg/L. Recommended serum sampling time at steady state: trough within 30 min before third consecutive dose and peak 30–60 minutes after administration of third consecutive dose. Peak levels of 25–30 mg/L have been recommended for CNS, pulmonary, bone, life-threatening, *Pseudomonas* infections, and in febrile neutropenic patients.

Therapeutic levels for cystic fibrosis using high-dose extended interval (once daily) dosing: Peak, 80 to 120 mg/L; trough, <10 mg/L. Recommended serum sampling time: trough within 30 minutes before dose and peak 30 to 60 minutes after administration of dose.

For initial dosing in obese patients, use an adjusted body weight (ABW). ABW = Ideal body weight + 0.4 (Total body weight – Ideal body weight).

May cause ototoxicity, nephrotoxicity, neuromuscular blockade, and rash. Loop diuretics may potentiate ototoxicity of all aminoglycoside antibiotics.

**AMINOCAPROIC ACID**

Amicar and generics

**Hemostatic agent**

Yes



Yes



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C

**Tabs:** 500, 1000 mg**Oral liquid/syrup:** 250 mg/mL (240, 480 mL); may contain 0.2% methylparaben and 0.05% propylparaben**Injection:** 250 mg/mL (20 mL); contains 0.9% benzyl alcohol**Child (IV/PO):****Loading dose:** 100–200 mg/kg**Maintenance:** 100 mg/kg/dose Q4–6 hr; **max. dose:** 30 g/24 hr**Adult (IV/PO):** 4–5 g during the first hour, followed by 1 g/hr  $\times$  8 hr or until bleeding is controlled.**Max. dose:** 30 g/24 hr

**Contraindications:** DIC, hematuria. **Use with caution** in patients with cardiac, renal, or hepatic disease. Should not be given with factor IX complex concentrates or antiinhibitor coagulant concentrates because of risk for thrombosis. Dose should be reduced by 75% in oliguria or end-stage renal disease. Hypercoagulation may be produced when given in conjunction with oral contraceptives.

May cause nausea, diarrhea, malaise, weakness, headache, decreased platelet function, hypotension, and false increase in urine amino acids. Elevation of serum potassium may occur, especially in patients with renal impairment.

**AMINOPHYLLINE**

Various generic products

**Bronchodilator, methylxanthine**

Yes



No



1



C

**Injection:** 25 mg/mL (79% theophylline) (10, 20 mL)**Note:** Pharmacy may dilute IV dosage forms to enhance accuracy of neonatal dosing.**Neonatal apnea:****Loading dose:** 5–6 mg/kg IV**Maintenance dose:** 1–2 mg/kg/dose Q6–8 hr, IV**Asthma exacerbation and reactive airway disease:****IV loading:** 6 mg/kg IV over 20 min (each 1.2 mg/kg dose raises the serum theophylline concentration 2 mg/L)**IV maintenance:** Continuous IV drip:**Neonate:** 0.2 mg/kg/hr**6 wk–6 mo:** 0.5 mg/kg/hr**6 mo–1 yr:** 0.6–0.7 mg/kg/hr**1–9 yr:** 1–1.2 mg/kg/hr**9–12 yr and young adult smoker:** 0.9 mg/kg/hr**>12 yr healthy nonsmoker:** 0.7 mg/kg/hrThe above total daily doses may also be administered IV  $\div$  Q4–6 hr.

Consider mg of theophylline available when dosing aminophylline. For oral route of administration, use theophylline.

Monitoring serum levels is essential, especially in infants and young children. Intermittent dosing for infants and children 1–5 yr may require Q4 hr dosing regimen owing to enhanced metabolism/clearance. Side effects: restlessness, GI upset, headache, tachycardia, seizures (may occur in absence of other side effects with toxic levels).

AMINOPHYLLINE *continued*

Therapeutic level (theophylline): For asthma, 10–20 mg/L; for neonatal apnea, 6–13 mg/L.

Recommended Guidelines for obtaining levels:

IV bolus: 30 min after infusion

IV continuous: 12–24 hr after initiation of infusion

PO liquid, immediate-release tab:

*Peak:* 1 hr post dose

*Trough:* Just before dose

PO sustained-release:

*Peak:* 4 hr post dose

*Trough:* Just before dose

Ideally, obtain levels after steady state has been achieved (after at least 1 day of therapy). Liver impairment, cardiac failure, and sustained high fever may increase theophylline levels. See *Theophylline* for drug interactions.

Use in breast-feeding may cause irritability in infant. It is recommended to avoid breast-feeding for 2 hr after IV or 4 hr after immediate-release oral intermittent dose.

**AMIODARONE HCL**

Cordarone, Pacerone, Nexterone, and various generics

**Antiarrhythmic, Class III**



Yes



No



3



D

**Tabs:** 100, 200, 400 mg

**Oral suspension:** 5 mg/mL 

**Injection:** 50 mg/mL (3, 9, 18 mL) (contains 20.2 mg/mL benzyl alcohol and 100 mg/mL polysorbate 80 or Tween 80)

**Premixed injection (Nexterone):** 1.5 mg/mL (100 mL) (iso-osmotic solution, each 1 mL contains 15 mg sulfobutyl ether  $\beta$ -cyclodextrin, 0.362 mg citric acid, 0.183 mg sodium citrate, and 42.1 mg dextrose), 1.8 mg/mL (200 mL) (iso-osmotic solution, each 1 mL contains 18 mg sulfobutyl ether  $\beta$ -cyclodextrin, 0.362 mg citric acid, 0.183 mg sodium citrate, and 41.4 mg dextrose)  
Contains 37% iodine by weight.

**See algorithms in front cover of book for arrest dosing.**

**Child PO for tachyarrhythmia:**

**<1 yr:** 600–800 mg/1.73 m<sup>2</sup>/24 hr  $\div$  Q12–24 hr  $\times$  4–14 days and/or until adequate control achieved, then reduce to 200–400 mg/1.73 m<sup>2</sup>/24 hr.

**$\geq 1$  yr:** 10–15 mg/kg/24 hr  $\div$  Q12–24 hr  $\times$  4–14 days and/or until adequate control achieved, then reduce to 5 mg/kg/24 hr  $\div$  Q12–24 hr if effective.

**Child IV for tachyarrhythmia (limited data):**

5 mg/kg (**max. dose:** 300 mg) over 30 min, followed by a continuous infusion starting at 5 mcg/kg/min; infusion may be increased up to a **max. dose** of 15 mcg/kg/min or 20 mg/kg/24 hr.

**Adult PO for ventricular arrhythmias:**

**Loading dose:** 800–1600 mg/24 hr  $\div$  Q12–24 hr for 1–3 wk

**Maintenance:** 600–800 mg/24 hr  $\div$  Q12–24 hr  $\times$  1 mo, then 200 mg Q12–24 hr

**Use lowest effective dose to minimize adverse reactions.**

**Adult IV for ventricular arrhythmias:**

**Loading dose:** 150 mg over 10 min (15 mg/min), followed by 360 mg over 6 hr (1 mg/min), followed by a maintenance dose of 0.5 mg/min. Supplemental boluses of 150 mg over 10 min may be given for breakthrough VF or hemodynamically unstable VT, and the maintenance infusion may be increased to suppress the arrhythmia. **Max. dose:** 2.1 g/24 hr.

*Continued*



AMIODARONE HCL *continued*

Used in the resuscitation algorithm for ventricular fibrillation/pulseless ventricular tachycardia (**see front cover for arrest dosing and back cover for PALS algorithm**).



Overall use of this drug may be limited to its potentially life-threatening side effects and the difficulties associated with managing its use.

**Contraindicated** in severe sinus node dysfunction, marked sinus bradycardia, second- and third-degree AV block. **Use with caution** in hepatic impairment.

Long elimination half-life (40–55 days). Major metabolite is active.

Increases cyclosporine, digoxin, phenytoin, tacrolimus, warfarin, calcium channel blocker, theophylline, and quinidine levels. Amiodarone is a cytochrome P450 3A3/4 substrate and inhibits CYP 3A3/4, 2C9, and 2D6. Risk of rhabdomyolysis is increased when used with simvastatin at doses >20 mg/24 hr and lovastatin at doses >40 mg/24 hr.

Proposed therapeutic level with chronic oral use: 1–2.5 mg/L.

Asymptomatic corneal microdeposits should appear in all patients. Alters liver enzymes, thyroid function. Pulmonary fibrosis reported in adults. May cause worsening of preexisting arrhythmias with bradycardia and AV block. May also cause hypotension, anorexia, nausea, vomiting, dizziness, paresthesias, ataxia, tremor, SIADH, and hypothyroidism or hyperthyroidism. Drug rash with eosinophilia and systemic symptoms (DRESS) have been reported.

Intravenous continuous infusion concentration for peripheral administration should not exceed 2 mg/mL and **must be diluted** with D<sub>5</sub>W. The intravenous dosage form can leach out plasticizers such as DEHP. To reduce potential exposure to plasticizers in pregnant women and children at the toddler stages of development and younger, alternative methods of IV drug administration should be used.

Oral administration should be consistent with regard to meals, because food increases the rate and extent of oral absorption.

**AMITRIPTYLINE**

Elavil and generics

**Antidepressant, tricyclic**



Yes



No



2



C

**Tabs:** 10, 25, 50, 75, 100, 150 mg

**Oral suspension:** 1 mg/mL 

**Antidepressant:**

**Child:** Start with 1 mg/kg/24 hr ÷ TID PO for 3 days; then increase to 1.5 mg/kg/24 hr.

Dose may be gradually increased to a **max. dose** of 5 mg/kg/24 hr if needed.

Monitor ECG, BP, and heart rate for doses >3 mg/kg/24 hr.

**Adolescent:** 10 mg TID PO and 20 mg QHS; dose may be gradually increased up to a **max. dose** of 200 mg/24 hr if needed.

**Adult:** 40–100 mg/24 hr ÷ QHS–BID PO; dose may be gradually increased up to 300 mg/24 hr if needed; gradually decrease dose to lowest effective dose when symptoms are controlled.

**Augment analgesia for chronic pain:**

**Child:** Initial 0.1 mg/kg/dose QHS PO; increase as needed and tolerated over 2–3 wk to 0.5–2 mg/kg/dose QHS.

**Migraine prophylaxis (limited data):**

**Child:** Initial 0.1–0.25 mg/kg/dose QHS PO; increase as needed and tolerated Q2 wk by 0.1–0.25 mg/kg/dose up to a **max. dose** of 2 mg/kg/24 hr or 75 mg/24 hr. For doses >1 mg/kg/24 hr, divide daily dose BID and monitor ECG.

**Adult:** Initial 10–25 mg/dose QHS PO; reported range of 10–400 mg/24 hr.

AMITRIPTYLINE *continued*

**Contraindicated** in narrow-angle glaucoma, seizures, severe cardiac disorders, and patients who received MAO inhibitors within 14 days.

$T_{1/2}$  = 9–25 hr in adults. Maximum antidepressant effects may not occur for 2 wk or more after initiation of therapy. **Do not abruptly discontinue therapy in patients receiving high doses for prolonged periods.**

Therapeutic levels (sum of amitriptyline and nortriptyline): 100–250 ng/mL. Recommended serum sampling time: obtain a single level 8 hr or more after an oral dose (after 4–5 days of continuous dosing). Amitriptyline is a substrate for CYP 450 1A2, 2C9, 2C19, 2D6, and 3A3/4 and inhibitor for CYP 450 1A2, 2C19, 2C9, 2D6, and 2E1. Rifampin can decrease amitriptyline levels. Amitriptyline may increase side effects of tramadol.

Side effects include sedation, urinary retention, constipation, dry mouth, dizziness, drowsiness, liver enzyme elevation, and arrhythmia. May discolor urine (blue/green). QHS dosing during first weeks of therapy will reduce sedation. Monitor ECG, BP, CBC at start of therapy and with dose changes. Decrease dose if PR interval reaches 0.22 sec, QRS reaches 130% of baseline, HR rises above 140/min, or if BP is >140/90. Tricyclics may cause mania. For antidepressant use, monitor for clinical worsening of depression and suicidal ideation/behavior after initiation of therapy or after dose changes.

**AMLODIPINE**

Norvasc

**Calcium channel blocker, antihypertensive**

Yes



No



?



C

**Tabs:** 2.5, 5, 10 mg

**Oral suspension:** 1 mg/mL 

**Child:**

**Hypertension:** Start with 0.1 mg/kg/dose (**max. dose:** 5 mg) PO once daily–BID; dosage may be gradually increased to a **max. dose** of 0.6 mg/kg/24 hr up to 20 mg/24 hr.

An effective antihypertensive dose for 6–17 year olds of 2.5–5 mg once daily has been reported; doses >5 mg have not been evaluated.

**Adult:**

**Hypertension:** 5–10 mg/dose once daily PO; use 2.5 mg/dose once daily PO in patients with hepatic insufficiency.

**Max. dose:** 10 mg/24 hr

**Use with caution** in combination with other antihypertensive agents. Younger children may require higher mg/kg doses than older children and adults. A BID dosing regimen may provide better efficacy in children.

Reduce dose in hepatic insufficiency. Allow 5–7 days of continuous initial dose therapy before making dosage adjustments because of the drug's gradual onset of action and lengthy elimination half-life. Amlodipine is a substrate for CYP 450 3A4 and **should be used with caution** with 3A4 inhibitors such as protease inhibitors and azole antifungals (e.g., fluconazole, ketoconazole). May increase levels and toxicity of cyclosporine and simvastatin.

Dose-related side effects include edema, dizziness, flushing, fatigue, and palpitations. Other side effects include headache, nausea, abdominal pain, and somnolence.

**AMMONIUM CHLORIDE**

Various generics

**Diuretic, urinary acidifying agent**

Yes



Yes



?



C

**Injection:** 5 mEq/mL (26.75%) (20 mL); contains EDTA

1 mEq = 53 mg

**Urinary acidification:****Child:** 75 mg/kg/24 hr ÷ Q6 hr IV; **max. dose:** 6 g/24 hr**Adult:** 1.5 g/dose Q6 hr IV**Drug administration:** Dilute to concentration  $\leq 0.4$  mEq/mL. Infusion **not to exceed** 50 mg/kg/hr or 1 mEq/kg/hr.**Contraindicated** in hepatic or renal insufficiency and primary respiratory acidosis.**Use with caution** in infants.

May produce acidosis, hyperammonemia, and GI irritation. Monitor serum chloride level, acid/base status, and serum ammonia.

**AMOXICILLIN**

Amoxil, Trimox, Wymox, Polymox, Moxatag and generics

**Antibiotic, aminopenicillin**

No



Yes



1



B

**Oral suspension:** 125, 250 mg/5 mL (80, 100, 150 mL); and 200, 400 mg/5 mL (50, 75, 100 mL)**Caps:** 250, 500 mg**Tablets:** 500, 875 mg**Chewable tabs:** 125, 200, 250, 400 mg; may contain phenylalanine**Extended-release tabs (Moxatag [see remarks]):** 775 mg**Neonate to  $\leq 3$  mo:** 20–30 mg/kg/24 hr ÷ Q12 hr PO**Child:****Standard dose:** 25–50 mg/kg/24 hr ÷ Q8–12 hr PO**High dose (resistant *Streptococcus pneumoniae*):** 80–90 mg/kg/24 hr ÷ BID PO**Max. dose:** 2–3 g/24 hr**Adult:****Mild/moderate infections:** 250 mg/dose Q8 hr PO OR 500 mg/dose Q12 hr PO**Severe infections:** 500 mg/dose Q8 hr PO OR 875 mg/dose Q12 hr PO**Max. dose:** 2–3 g/24 hr**Tonsillitis/pharyngitis (*Streptococcus pyogenes*):** 50 mg/kg/24 hr ÷ Q12 hr PO  $\times 10$  days; **max. dose:** 1 g/24 hr.**Extended-release tablets (Moxatag):** 775 mg once daily PO  $\times 10$  days is indicated for children  $\geq 12$  yr and adults.**Recurrent otitis media prophylaxis:** 20 mg/kg/dose QHS PO**SBE prophylaxis:** See Chapter 7.**Early Lyme disease:****Child:** 50 mg/kg/24 hr ÷ Q8 hr PO  $\times 14$ –21 days; **max. dose:** 1.5 g/24 hr**Adult:** 500 mg/dose Q8 hr PO  $\times 14$ –21 daysRenal elimination. **Adjust dose in renal failure (see Chapter 31).** Serum levels about twice those achieved with equal dose of ampicillin. Fewer GI effects but otherwise similar to ampicillin. Side effects: rash and diarrhea. Rash may develop with concurrent EBV infection. May increase warfarin's effect by increasing INR.

High-dose regimen, increasingly useful, is recommended in respiratory infections, acute otitis media, and sinusitis, owing to increasing incidence of penicillin-resistant pneumococci. Chewable tablets may contain phenylalanine and should not be used by phenylketonurics.

**AMOXICILLIN–CLAVULANIC ACID**

Augmentin, Amoclan, Augmentin ES-600, Augmentin XR, and various generic products

**Antibiotic, aminopenicillin with  $\beta$ -lactamase inhibitor**



No



Yes



1



B

**Tabs:**

**For TID dosing:** 250, 500 mg (with 125 mg clavulanate)

**For BID dosing:** 875 mg amoxicillin (with 125 mg clavulanate); Augmentin XR: 1 g amoxicillin (with 62.5 mg clavulanate)

**Chewable tabs:**

**For BID dosing:** 200, 400 mg amoxicillin (28.5 and 57 mg clavulanate, respectively); contains saccharin and aspartame

**Oral suspension:**

**For TID dosing:** 125, 250 mg amoxicillin/5 mL (31.25 and 62.5 mg clavulanate/5 mL, respectively) (75, 100, 150 mL); contains saccharin

**For BID dosing:** 200, 400 mg amoxicillin/5 mL (28.5 and 57 mg clavulanate/5 mL, respectively) (50, 75, 100 mL); 600 mg amoxicillin/5 mL (Augmentin ES-600 contains 42.9 mg clavulanate/5 mL) (50, 75, 125, 200 mL); contains saccharin and/or aspartame

Contains 0.63 mEq K<sup>+</sup> per 125 mg clavulanate (Augmentin ES-600 contains 0.23 mEq K<sup>+</sup> per 42.9 mg clavulanate)

**Dosage based on amoxicillin component (see remarks for resistant *S. pneumoniae*).**

**Infant 1–<3 mo:** 30 mg/kg/24 hr ÷ Q12 hr PO (recommended dosage form is 125 mg/5 mL suspension)

**Child ≥3 mo:**

**TID dosing (see remarks):** 20–40 mg/kg/24 hr ÷ Q8 hr PO

**BID dosing (see remarks):** 25–45 mg/kg/24 hr ÷ Q12 hr PO

**Augmentin ES-600:**

**≥3 mo and <40 kg:** 90 mg/kg/24 hr ÷ Q12 hr PO × 10 days

**Adult:** 250–500 mg/dose Q8 hr PO or 875 mg/dose Q12 hr PO for more severe and respiratory infections

**Augmentin XR:**

**≥16 yr and adult:** 2 g Q12 hr PO × 10 days for acute bacterial sinusitis or × 7–10 days for community-acquired pneumonia

Clavulanic acid extends the activity of amoxicillin to include  $\beta$ -lactamase–producing strains of *Haemophilus influenzae*, *Moraxella catarrhalis*, *Neisseria gonorrhoeae*, and some *Staphylococcus aureus* and may increase the risk for diarrhea. See *Amoxicillin* for additional comments. **Adjust dose in renal failure (see Chapter 31).** **Contraindicated** in patients with a history of cholestatic jaundice/hepatic dysfunction associated with amoxicillin–clavulanic acid. Augmentin XR is **contraindicated** in patients with CrCl <30 mL/min.



The BID dosing schedule is associated with less diarrhea. For BID dosing, the 875-mg, 1-g tablets; the 200-mg, 400-mg chewable tablets; or the 200-mg/5 mL, 400-mg/5 mL, 600-mg/5 mL suspensions should be used. These BID dosage forms contain phenylalanine and **should not be used** by phenylketonurics. For TID dosing, the 250-mg, 500-mg tablets; or the 125-mg/5 mL, 250-mg/5 mL suspensions should be used.

Higher doses of 80–90 mg/kg/24 hr (amoxicillin component) have been recommended for resistant strains of *S. pneumoniae* in acute otitis media (use BID formulations containing 7:1 ratio of amoxicillin to clavulanic acid or Augmentin ES-600).

The 250 or 500 mg tablets **cannot** be substituted for Augmentin XR.

**AMPHOTERICIN B (CONVENTIONAL)**

Fungizone, Amphocin, and various generics

**Antifungal, polyene**

Yes



Yes



?



B

**Injection:** 50-mg vials**IV:** Mix with D<sub>5</sub>W to concentration 0.1 mg/mL (peripheral administration) or 0.25 mg/mL (central line only). pH > 4.2. Infuse over 2–6 hr.**Optional test dose:** 0.1 mg/kg/dose IV up to **max. dose** of 1 mg (followed by remaining initial dose).**Initial dose:** 0.5–1 mg/kg/24 hr; if test dose NOT used, infuse first dose over 6 hr and monitor frequently during the first several hours.**Increment:** Increase as tolerated by 0.25–0.5 mg/kg/24 hr once daily or every other day. Use larger dosage increment (0.5 mg once daily) for critically ill patients.**Usual maintenance:****Once-daily dosing:** 0.5–1 mg/kg/24 hr once daily**Every-other-day dosing:** 1.5 mg/kg/dose every other day**Max. dose:** 1.5 mg/kg/24 hr**Intrathecal:** 25–100 mcg Q48–72 hr. Increase to 500 mcg as tolerated.**Bladder irrigation for urinary tract mycosis:** 5–15 mg in 100 mL sterile water for irrigation at 100–300 mL/24 hr. Instill solution into bladder, clamp catheter for 1–2 hr, then drain; repeat TID–QID for 2–5 days.Monitor renal, hepatic, electrolyte, and hematologic status closely. Hypercalciuria, hypokalemia, hypomagnesemia, RTA, renal failure, acute hepatic failure, hypotension, and phlebitis may occur. **For dosing information in renal failure, see Chapter 31.**Common infusion-related reactions include fever, chills, headache, hypotension, nausea, vomiting; may premedicate with acetaminophen and diphenhydramine 30 min before and 4 hr after infusion. Meperidine useful for chills. Hydrocortisone, 1 mg/kg amphi (**max. dose:** 25 mg) added to bottle may help prevent immediate adverse reactions. Use total body weight for obese patients when calculating dosages.

Salt loading with 10–15 mL/kg of NS infused before each dose may minimize the risk of nephrotoxicity.

Maintaining sodium intake of &gt;4/kg/24 hr in premature neonates may also reduce risk for nephrotoxicity. Nephrotoxic drugs (e.g., aminoglycosides, chemotherapeutic agents, cyclosporine) may result in synergistic toxicity. Hypokalemia may increase toxicity of neuromuscular blocking agents and cardiac glycosides.

**AMPHOTERICIN B LIPID COMPLEX**

Abelcet, ABLC

**Antifungal, polyene**

Yes



Yes



?



B

**Injection:** 5 mg/mL (20 mL)

(formulated as a 1:1 molar ratio of amphotericin B to lipid complex composed of dimyristoylphosphatidylcholine and dimyristoylphosphatidylglycerol)

**IV:** 2.5–5 mg/kg/24 hr once daily

For visceral leishmaniasis that failed to respond to or relapsed after treatment with antimony compound, a dosage of 1–3 mg/kg/24 hr once daily × 5 days has been used.

Mix with D<sub>5</sub>W to concentration 1 or 2 mg/mL for fluid-restricted patients.**Infusion rate:** 2.5 mg/kg/hr; shake infusion bag Q2 hr if total infusion time exceeds 2 hr. **Do not use** an in-line filter.

Monitor renal, hepatic, electrolyte, and hematologic status closely. Thrombocytopenia, anemia, leukopenia, hypokalemia, hypomagnesemia, diarrhea, respiratory failure, rash, nephrotoxicity, and increases in liver enzymes and bilirubin may occur. See conventional amphotericin for drug interactions.

AMPHOTERICIN B LIPID COMPLEX *continued*

Highest concentrations achieved in spleen, lung, and liver from human autopsy data from one heart transplant patient. CNS/CSF levels are lower than amphotericin B, liposomal (AmBisome). In animal models, concentrations are higher in the liver, spleen, and lungs but the same in the kidneys when compared with conventional amphotericin B. Pharmacokinetics in renal and hepatic impairment have not been studied.

Common infusion-related reactions include fever, chills, rigors, nausea, vomiting, hypotension, and headache; may premedicate with acetaminophen, diphenhydramine, and meperidine (see *Amphotericin B* remarks).

**AMPHOTERICIN B, LIPOSOMAL**

AmBisome

**Antifungal, polyene**

Yes



Yes



?



B

**Injection:** 50 mg (vials); contains soy, 900 mg sucrose (formulated in liposomes composed of hydrogenated soy phosphatidylcholine, cholesterol, distearoylphosphatidylglycerol, and  $\alpha$ -tocopherol)

**Systemic fungal infections:** 3–5 mg/kg/24 hr IV once daily; an upper dosage limit of 10 mg/kg/24 hr has been suggested based on pharmacokinetic endpoints and risk for hypokalemia. However, dosages as high as 15 mg/kg/24 hr have been used. Dosages as high as 10 mg/kg/24 hr have been used in patients with *Aspergillus*.



**Empirical therapy for febrile neutropenia:** 3 mg/kg/24 hr IV once daily

**Cryptococcal meningitis in HIV:** 6 mg/kg/24 hr IV once daily

**Leishmaniasis (a repeat course may be necessary if infection does not clear):**

**Immunocompetent:** 3 mg/kg/24 hr IV on days 1 to 5, 14, and 21

**Immunocompromised:** 4 mg/kg/24 hr IV on days 1 to 5, 10, 17, 24, 31, and 38

Mix with D<sub>5</sub>W to concentration of 1–2 mg/mL (0.2–0.5 mg/mL may be used for infants and small children).

**Infusion rate:** Administer dose over 2 hr; infusion may be reduced to 1 hr if well tolerated. A  $\geq 1$ -micron in-line filter may be used.

Closely monitor renal, hepatic, electrolyte, and hematologic status. Thrombocytopenia, anemia, leukopenia, tachycardia, hypokalemia, hypomagnesemia, hypocalcemia, hyperglycemia, diarrhea, dyspnea, rash, low back pain, nephrotoxicity, and increases in liver enzymes and bilirubin may occur. Rhabdomyolysis has been reported. Safety and effectiveness in neonates have not been established. See conventional *Amphotericin* for drug interactions.



Compared with conventional amphotericin B, higher concentrations found in liver and spleen; similar concentrations found in lungs and kidneys. CNS/CSF concentrations are higher than other amphotericin B products. Pharmacokinetics in renal and hepatic impairment have not been studied. Common infusion-related reactions include fever, chills, rigors, nausea, vomiting, hypotension, and headache; may premedicate with acetaminophen, diphenhydramine, and meperidine (see *Amphotericin B* remarks).

False elevations of serum phosphate have been reported with the PHOSm assay (used in Beckman Coulter analyzers).

**AMPICILLIN**

Omnipen, Principen, Totacillin, and generics

**Antibiotic, aminopenicillin**

No



Yes



1



B

**Oral suspension:** 125 mg/5 mL, 250 mg/5 mL (100, 200 mL)**Caps:** 250, 500 mg**Injection:** 125, 250, 500 mg; 1, 2, 10 g

Contains 3 mEq Na/1 g IV drug

**Neonate (IM/IV):****<7 days:****<2 kg:** 50–100 mg/kg/24 hr ÷ Q12 hr**≥2 kg:** 75–150 mg/kg/24 hr ÷ Q8 hr**Group B streptococcal meningitis:** 200–300 mg/kg/24 hr ÷ Q8 hr**≥7 days:****<1.2 kg:** 50–100 mg/kg/24 hr ÷ Q12 hr**1.2–2 kg:** 75–150 mg/kg/24 hr ÷ Q8 hr**>2 kg:** 100–200 mg/kg/24 hr ÷ Q6 hr**Group B streptococcal meningitis:** 300 mg/kg/24 hr ÷ Q4–6 hr**Infant/child:****Mild/moderate infections:****IM/IV:** 100–200 mg/kg/24 hr ÷ Q6 hr**PO:** 50–100 mg/kg/24 hr ÷ Q6 hr; **max. PO dose:** 2–3 g/24 hr**Severe infections:** 200–400 mg/kg/24 hr ÷ Q4–6 hr IM/IV**Community-acquired pneumonia in a fully immunized patient (IV/IM):****Streptococcus pneumoniae penicillin MIC ≤ 2.0:** 150–200 mg/kg/24 hr ÷ Q6 hr**Streptococcus pneumoniae penicillin MIC ≥ 4.0:** 300–400 mg/kg/24 hr ÷ Q6 hr**Max. IV/IM dose:** 12 g/24 hr**Adult:****IM/IV:** 500–3000 mg Q4–6 hr**PO:** 250–500 mg Q6 hr**Max. IV/IM dose:** 14 g/24 hr**SBE prophylaxis:****Moderate-risk patients:****Child:** 50 mg/kg/dose × 1 IV/IM 30 min before procedure; **max. dose:** 2 g/dose**Adult:** 2 g/dose × 1 IV/IM 30 min before procedure**High-risk patients with GU and GI procedures:** Above doses PLUS gentamicin 1.5 mg/kg × 1 (max. dose: 120 mg) IV within 30 min of starting procedure.

Use higher doses with shorter dosing intervals to treat CNS disease and severe infection.

CSF penetration occurs only with inflamed meninges. **Adjust dose in renal failure** (see Chapter 31).

Produces the same side effects as penicillin, with cross-reactivity. Rash commonly seen at 5–10 days, and rash may occur with concurrent EBV infection or allopurinol use. May cause interstitial nephritis, diarrhea, and pseudomembranous enterocolitis. Chloroquine reduces ampicillin's oral absorption.

**AMPICILLIN/SULBACTAM**

Unasyn and generics

**Antibiotic, aminopenicillin with  $\beta$ -lactamase inhibitor**

No



Yes



1



B

**Injection:**

1.5 g = ampicillin 1 g + sulbactam 0.5 g

3 g = ampicillin 2 g + sulbactam 1 g

15 g = ampicillin 10 g + sulbactam 5 g

Contains 5 mEq Na per 1.5 g drug combination

**Dosage based on ampicillin component:****Neonate:****Premature (based on pharmacokinetic data):** 100 mg/kg/24 hr  $\div$  Q12 hr IM/IV**Full-term:** 100 mg/kg/24 hr  $\div$  Q8 hr IM/IV**Infant  $\geq$  1 mo:****Mild/moderate infections:** 100–150 mg/kg/24 hr  $\div$  Q6 hr IM/IV**Meningitis/severe infections:** 200–300 mg/kg/24 hr  $\div$  Q6 hr IM/IV**Child:****Mild/moderate infections:** 100–200 mg/kg/24 hr  $\div$  Q6 hr IM/IV**Meningitis/severe infections:** 200–400 mg/kg/24 hr  $\div$  Q4–6 hr IM/IV**Adult:** 1–2 g Q6–8 hr IM/IV**Max. dose:** 8 g ampicillin/24 hr

Similar spectrum of antibacterial activity to ampicillin, with the added coverage of  $\beta$ -lactamase–producing organisms. Total sulbactam dose should not exceed 4 g/24 hr. Use higher doses with shorter dosing intervals to treat CNS disease and severe infection.

**Adjust dose in renal failure (see Chapter 31).** CSF distribution and side effects similar to ampicillin.

**ANTIPYRINE AND BENZOCAINE (OTIC)**

Allergen Ear Drops, Antipyrine and Benzocaine Otic, Aurodex, Autoguard Otic, Auralgan (available in Canada), and generics

**Otic analgesic, cerumenolytic**

No



No



2



C

**Otic solution:** Antipyrine 5.4%, benzocaine 1.4% (10, 15 mL); may contain oxyquinoline sulfate

**Otic analgesia:** Fill external ear canal (2–4 drops) Q1–2 hr PRN. After instillation of solution, a cotton pledget should be moistened with solution and inserted into the meatus.

**Cerumenolytic:** Fill external ear canal (2–4 drops) TID–QID for 2–3 days.

Benzocaine sensitivity may develop; not intended for prolonged use. **Contraindicated** if tympanic membrane perforated or PE tubes in place. Local reactions (e.g., burning, stinging) and hypersensitivity reactions may occur. Risk of benzocaine-induced methemoglobinemia may be increased in infants  $\leq$ 3 mo of age.



**ARGININE CHLORIDE—INJECTABLE PREPARATION**

R-Genex 10

**Metabolic alkalosis agent, urea cycle disorder treatment agent, growth hormone diagnostic agent**

Yes



Yes



?



B

**Injection:** 10% (100 mg/mL) arginine hydrochloride contains 47.5 mEq chloride per 100 mL (300 mL)**Osmolality:** 950 mOsmol/L**Used as a secondary alternative agent for patients who are unresponsive or unable to receive sodium chloride and potassium chloride.****Correction of hypochloremia:** Arginine chloride dose in mEq =  $0.2 \times \text{Patient's weight (kg)} \times [103 - \text{Patient's serum chloride in mEq/L}]$ . Administer  $\frac{1}{2}$  to  $\frac{3}{4}$  of the calculated dose and reassess.**Drug administration:** Do not exceed an IV infusion rate of 1 g/kg/hr (4.75 mEq/kg/hr). Drug may be administered without further dilution but should be diluted to reduce risk of tissue irritation.**Contraindicated** in renal or hepatic failure. **Use with extreme caution;** overdoses may result in hyperchloremic metabolic acidosis, cerebral edema, and death. Hypersensitivity reactions, including anaphylaxis, and hematuria have been reported.

Arginine hydrochloride is metabolized to nitrogen-containing products for renal excretion. Excess arginine increases production of nitric oxide (NO) to cause vasodilation/hypotension. Closely monitor acid-base status. Hyperglycemia, hyperkalemia, GI disturbances, IV extravasation, headache, and flushing may occur. In addition to its use for chloride supplementation, arginine is used in urea cycle disorder therapy (to increase arginine levels and prevent breakdown of endogenous proteins) and as a diagnostic agent for growth hormone (stimulates pituitary release of growth hormone).

**ASCORBIC ACID**

Vitamin C, Sunkist Vitamin C, and many others

**Water-soluble vitamin**

No



No



1



A/C

**Tabs [OTC]:** 100, 250, 500 mg, 1 g**Chewable tabs (Sunkist Vitamin C and others) [OTC]:** 100, 250, 500 mg; some may contain aspartame**Tabs (timed-release) [OTC]:** 0.5, 1, 1.5 g**Caps [OTC]:** 500, 1000 mg**Extended-release caps [OTC]:** 500 mg**Injection:** 500 mg/mL; may contain sodium hydrosulfite**Oral liquid [OTC]:** 500 mg/5 mL (120, 480 mL)**Crystals [OTC]:** 1 g per  $\frac{1}{4}$  teaspoonful (170 g, 1000 g)Some products may contain  $\approx 5$  mEq Na/1 g drug and/or calcium.**Scurvy (PO/IM/IV/SC):****Child:** 100–300 mg/24 hr  $\div$  once daily–BID for at least 2 wk**Adult:** 100–250 mg once daily–BID for at least 2 wk**U.S. Recommended Daily Allowance (RDA):**

See Chapter 21.

Adverse reactions: Nausea, vomiting, heartburn, flushing, headache, faintness, dizziness, hyperoxaluria. Use high doses with **caution** in G6PD patients. May cause false-negative and false-positive urine glucose determinations with glucose oxidase and cupric sulfate tests, respectively.



May increase absorption of aluminum hydroxide and increase adverse/toxic effects of deferoxamine.

May reduce effects of amphetamines.

Oral dosing is preferred with or without food. IM route is the preferred parenteral route. Protect the injectable dosage form from light.

Pregnancy Category changes to “C” if used in doses above the RDA.

**ASPIRIN**

ASA, Anacin, Bufferin, and various trade names and generics

**Nonsteroidal anti-inflammatory agent, antiplatelet agent, analgesic**

Yes



Yes



2



D

**Tab** [OTC]: 325, 500 mg**Tab**, enteric-coated [OTC]: 81, 325, 500, 650 mg**Tab**, time-release [OTC]: 81, 650 mg**Tab**, buffered [OTC]: 325, 500 mg; may contain magnesium, aluminum, and/or calcium**Tab**, chewable [OTC]: 81 mg**Gum** [OTC]: 227.5 mg (12s)**Suppository** [OTC]: 300, 600 mg**Analgesic/antipyretic:** 10–15 mg/kg/dose PO/PR Q4–6 hr up to total of 60–80 mg/kg/24 hr**Max. dose:** 4 g/24 hr**Anti-inflammatory:** 60–100 mg/kg/24 hr PO ÷ Q6–8 hr**Kawasaki disease:** 80–100 mg/kg/24 hr PO ÷ QID during febrile phase until patient defervesces, then decrease to 3–5 mg/kg/24 hr PO QAM. Continue for at least 8 wk or until both platelet count and ESR are normal.**Do not use in children <16 yr** for treatment of varicella or flulike symptoms (risk for Reye syndrome), in combination with other NSAIDs, or in severe renal failure. **Use with caution** in bleeding disorders, renal dysfunction, gastritis, and gout. May cause GI upset, allergic reactions, liver toxicity, and decreased platelet aggregation.**Drug interactions:** May increase effects of methotrexate, valproic acid, and warfarin, which may lead to toxicity (protein displacement). Buffered dosage forms may decrease absorption of ketoconazole and tetracycline. GI bleeds have been reported with concurrent use of SSRIs (e.g., fluoxetine, paroxetine, sertraline).Therapeutic levels: Antipyretic/analgesic, 30–50 mg/L; anti-inflammatory, 150–300 mg/L. Tinnitus may occur at levels of 200–400 mg/L. Recommended serum sampling time at steady state; obtain trough level just before dose after 1–2 days of continuous dosing. Peak levels obtained 2 hr (for non–sustained-release dosage forms) after a dose may be useful for monitoring toxicity. **Adjust dose in renal failure (see Chapter 31).**

Breast-feeding considerations:

High-dose aspirin regimens: Use of an alternative drug is recommended.

Low-dose (75–162 mg/24 hr) aspirin regimens: Avoid breast-feeding for 1–2 hr after a dose.

**ATENOLOL**

Tenormin and various generics

 **$\beta_1$ -Adrenergic blocker, selective**

No



Yes



2



D

**Tab:** 25, 50, 100 mg**Oral suspension:** 2 mg/mL **Child and adolescent:** 0.5–1 mg/kg/dose PO once daily–BID; **max. dose:** 2 mg/kg/24 hr up to 100 mg/24 hr**Adult:****PO:** 25–100 mg/dose PO once daily; **max. dose:** 100 mg/24 hr**Contraindicated** in pulmonary edema, cardiogenic shock. May cause bradycardia, hypotension, second- or third-degree AV block, dizziness, fatigue, lethargy, and headache. **Use with caution** in diabetes and asthma. Wheezing and dyspnea have occurred when daily dosage exceeds

Continued

ATENOLOL *continued*

100 mg/24 hr. Postmarketing evaluation reports a temporal relationship for causing elevated LFTs and/or bilirubin, hallucinations, psoriatic rash, thrombocytopenia, visual disturbances, and dry mouth. **Avoid** abrupt withdrawal of the drug. Does not cross the blood-brain barrier; lower incidence of CNS side effects compared with propranolol. Neonates born to mothers receiving atenolol during labor or while breast-feeding may be at risk for hypoglycemia.

Use with disopyramide, amiodarone, or digoxin may enhance bradycardic effects. **Adjust dose in renal impairment (see Chapter 31).**

**ATOMOXETINE**

Strattera

**Norepinephrine reuptake inhibitor, attention deficit hyperactivity disorder agent**



Yes



No



3



C

**Capsules:** 10, 18, 25, 40, 60, 80, 100 mg

**Child ≥ 6 yr and adolescent ≤ 70 kg (see remarks):**

Start with 0.5 mg/kg/24 hr PO QAM and increase after a minimum of 3 days to ≈ 1.2 mg/kg/24 hr PO ÷ QAM or BID (morning and late afternoon/early evening).

**Max. daily dose:** 1.4 mg/kg/24 hr or 100 mg, whichever is less

**If used with a strong CYP 450 2D6 inhibitor (e.g., fluoxetine, paroxetine, quinidine) or in patients with reduced CYP 450 2D6 activity:** Maintain above initial dose for 4 wk, and increase to a max. of 1.2 mg/kg/24 hr only if symptoms do not improve and initial dose is tolerated.

**Child ≥ 6 yr and adolescent > 70 kg (see remarks):**

Start with 40 mg PO QAM and increase after a minimum of 3 days to ≈ 80 mg/24 hr PO ÷ QAM or BID (morning and late afternoon/early evening). After 2–4 wk, dose may be increased to a **max.** of 100 mg/24 hr if needed.

**If used with a strong CYP 450 2D6 inhibitor (e.g., fluoxetine, paroxetine, quinidine) or in patients with reduced CYP 450 2D6 activity:** Maintain above initial dose for 4 wk, and increase to 80 mg/24 hr only if symptoms do not improve and initial dose is tolerated.

**Contraindicated** in patients with narrow-angle glaucoma, pheochromocytoma, and severe cardiac disorders. **Do not** administer with or within 2 wk after discontinuing an MAO inhibitor; fatal reactions have been reported. **Use with caution** in hypertension, tachycardia, cardiovascular or cerebrovascular diseases, or with concurrent albuterol therapy. Increased risk of suicidal thinking has been reported; closely monitor for clinical worsening, agitation, aggressive behavior, irritability, suicidal thinking or behaviors, and unusual changes in behavior when initiating (first few months) or at times of dose changes (increases or decreases). Atomoxetine is a CYP 450 2D6 substrate.

Doses > 1.2 mg/kg/24 hr in patients ≤ 70 kg have not been shown to be of additional benefit. Reduce dose (initial and target doses) by 50% and 75% for patients with moderate (Child-Pugh Class B) and severe (Child-Pugh Class C) hepatic insufficiency, respectively. Effectiveness beyond 9 weeks and safety beyond 1 year have not been evaluated by controlled trials in children.

Major side effects include GI discomfort, vomiting, fatigue, anorexia, dizziness, and mood swings.

Hypersensitivity reactions, aggression, irritability, allergic reactions, and severe liver injury have also been reported. Consider interrupting therapy in patients who are not growing or gaining weight satisfactorily.

Doses may be administered with or without food. Atomoxetine can be discontinued without tapering.

**ATOVAQUONE**

Meproon

**Antiprotozoal**

Yes



Yes



3



C

**Oral suspension:** 750 mg/5 mL (210 mL); contains benzyl alcohol**Pneumocystis jirovecii (carinii) pneumonia (PCP):****Treatment (21-day course):****Child:** 30–40 mg/kg/24 hr PO ÷ BID with fatty foods; **max. dose:** 1500 mg/24 hr. Infants 3–24 mo may require higher doses of 45 mg/kg/24 hr.**Adult:** 750 mg/dose PO BID**Prophylaxis (first episode and recurrence):****Child 1–3 mo or >24 mo:** 30 mg/kg/24 hr PO once daily; **max. dose:** 1500 mg/24 hr**Child 4–24 mo:** 45 mg/kg/24 hr PO once daily; **max. dose:** 1500 mg/24 hr**Adult:** 1500 mg/dose PO once daily**Toxoplasma gondii:****Child:****First episode prophylaxis and recurrence prophylaxis:** Use PCP prophylaxis dosages ± pyrimethamine 1 mg/kg/dose (**max.** 25 mg/dose) PO once daily PLUS leucovorin 5 mg PO Q3 days.**Adult:****Treatment:** 1500 mg/dose PO BID ± (sulfadiazine 1000–1500 mg PO Q6 hr or pyrimethamine PLUS leucovorin).**First episode prophylaxis:** 1500 mg/dose PO once daily ± pyrimethamine 25 mg PO once daily PLUS leucovorin 10 mg PO once daily.**Recurrence prophylaxis:** 750 mg/dose PO Q6–12 hr ± pyrimethamine 25 mg PO once daily PLUS leucovorin 10 mg PO once daily.**Not recommended** in the treatment of severe PCP (lack of clinical data). Patients with GI disorders or severe vomiting and who cannot tolerate oral therapy should consider alternative IV therapies. Rash, pruritus, sweating, GI symptoms, LFT elevation, dizziness, headache, insomnia, anxiety, cough, and fever are common. Anemia, Stevens-Johnson syndrome, hepatitis, renal/urinary disorders, and pancreatitis have been reported.

Metoclopramide, rifampin, rifabutin, and tetracycline may decrease atovaquone levels. Shake oral suspension well before dispensing all doses. Take all doses with high-fat foods to maximize absorption.

**ATROPINE SULFATE**

Sal-Tropine, AtroPen, and many other generic products

**Anticholinergic agent**

No



No



2



C

**Tabs (Sal-Tropine):** 0.4 mg**Injection:** 0.05, 0.1, 0.4, 0.8, 1 mg/mL**Injection (auto-injector):****AtroPen 0.25 mg:** Delivers a single 0.25-mg (0.3 mL) dose (yellow-colored pen)**AtroPen 0.5 mg:** Delivers a single 0.5-mg (0.7 mL) dose (blue-colored pen)**AtroPen 1 mg:** Delivers a single 1-mg (0.7 mL) dose (dark red-colored pen)**AtroPen 2 mg:** Delivers a single 2-mg (0.7 mL) dose (green-colored pen)**Ointment (ophthalmic):** 1% (1, 3.5 g)**Solution (ophthalmic):** 1% (2, 5, 15 mL)

Continued

ATROPINE SULFATE *continued***Preintubation dose:**

**Neonate:** 0.01–0.02 mg/kg/dose IV (over 1 min)/IM prior to other premedications.

**Child:** 0.01 mg/kg/dose IV/IM, **min. dose:** 0.1 mg/dose; **max. dose:** 0.4 mg/dose; may repeat Q4–6 hr PRN

**Adult:** 0.5 mg/dose IV/IM

**Cardiopulmonary resuscitation/bradycardia (see remarks):**

**Neonate:** 0.01–0.03 mg/kg/dose IV/IM Q10–15 min PRN up to a total **maximum** of 0.04 mg/kg. Administer IV over 1 min.

**Child:** 0.02 mg/kg/dose IV Q5 min  $\times$  2–3 doses PRN; **min. dose:** 0.1 mg/dose; **max. single dose:** 0.5 mg in children, 1 mg in adolescents; **max total dose:** 1 mg children, 2 mg adolescents

**Adult:** 0.5–1 mg/dose IV Q5 min; **max. total dose:** 2 mg

**Bronchospasm:** 0.025–0.05 mg/kg/dose (**max. dose:** 2.5 mg/dose) in 2.5 mL NS Q6–8 hr via nebulizer

**Nerve agent and insecticide poisoning for muscarinic symptoms (organophosphate or carbamate poisoning) (IV/IM/ET; dilute in 1–2 mL NS for ET administration):**

**Child:** 0.05–0.1 mg/kg Q5–10 min until bronchial or oral secretions terminate

**Adult:** 2–5 mg/dose Q5–10 min until bronchial or oral secretions terminate

**AtroPen device (IM route):** Inject as soon as exposure is known or suspected. Give 1 dose for mild symptoms and 2 additional doses (total 3 doses) in rapid succession 10 min after the first dose for severe symptoms as follows:

**Child < 6 mo (<7 kg):** 0.25 mg

**Child 6 mo–4 yr (7–18 kg):** 0.5 mg

**Child 4–10 yr (18–41 kg):** 1 mg

**Child > 10 yr and adult ( $\geq 41$  kg):** 2 mg

**Ophthalmic (uveitis):**

**Child:** (0.5% solution; prepared by diluting equal volume of the 1% atropine ophthalmic solution with artificial tears) 1–2 drops in each eye once daily–TID

**Adult:** (1% solution) 1–2 drops in each eye once daily–QID

**Contraindicated** in glaucoma, obstructive uropathy, tachycardia, and thyrotoxicosis. **Use with caution** in patients sensitive to sulfites.



Recommended minimum dosage of 0.1 mg for neonates for bradycardia is currently recommended by PALS for concerns of paradoxical bradycardia. However, use of this minimum dose could result in an overdose. Additionally, data suggest the minimum 0.1 mg dose may not be warranted for the pre-intubation indication as well.

Side effects include dry mouth, blurred vision, fever, tachycardia, constipation, urinary retention, CNS signs (dizziness, hallucinations, restlessness, fatigue, headache).

In case of bradycardia, may give via endotracheal tube (dilute with NS to volume of 1–2 mL and follow each dose with 1 mL NS) or intraosseous (IO) route. Use injectable solution for nebulized use; can be mixed with albuterol for simultaneous administration.

**AURALGAN**

See Antipyrine and Benzocaine

**AZATHIOPRINE**

Imuran, Azasan, and generics

**Immunosuppressant**

Yes



Yes



3



D

**Oral suspension:** 50 mg/mL **Tablets:****Imuran and generics:** 50 mg (scored)**Azasan:** 75, 100 mg (scored)**Injection:** 100 mg (20 mL)**Immunosuppression:****Child and adult:****Initial:** 3–5 mg/kg/24 hr IV/PO once daily**Maintenance:** 1–3 mg/kg/24 hr IV/PO once daily

Increased risk for hepatosplenic T-cell lymphoma has been reported in adolescents and young adults. Toxicity: bone marrow suppression, rash, stomatitis, hepatotoxicity, alopecia, arthralgias, and GI disturbances.



Use  $\frac{1}{4}$ – $\frac{1}{2}$  dose when given with allopurinol. Dose reduction or discontinuance is recommended in patients with low or absent thiopurine methyl transferase (TPMT) activity. Severe anemia has been reported when used in combination with captopril or enalapril. Monitor CBC, platelets, total bilirubin, alkaline phosphatase, BUN, and creatinine. Pancytopenia and bone marrow suppression have been reported with concomitant use of pegylated interferon and ribavirin in patients with hepatitis C.

**Adjust dose in renal failure (see Chapter 31).**

Administer oral doses with food to minimize GI discomfort. To minimize infant exposure via breast milk, avoid breast-feeding for 4–6 hr after administering a maternal dose.

**AZELASTINE**

Astelin, Astepro, Opatvar, and generics

**Antihistamine**

Yes



Yes



?



C

**Nasal spray:**

0.1% (Astelin, Astepro): 137 mcg/spray (200 actuations per 30 mL); contains benzalkonium chloride and EDTA

0.15% (Astepro): 205.5 mcg/spray (200 actuations per 30 mL); contains benzalkonium chloride and EDTA

**Ophthalmic drops (Opatvar):** 0.05% (0.5 mg/mL) (6 mL); contains benzalkonium chloride**Seasonal allergic rhinitis:****0.1% strength:****Child 5–11 yr:** 1 spray each nostril BID**≥12 yr and adult:** 1–2 sprays each nostril BID**0.15% strength:** Use similar dosing for 0.1% strength, or 2 sprays per nostril once daily for only children ≥12 yr and adults.**Ophthalmic:****≥3 yr and adult:** Instill 1 drop into each affected eye BID.

**Use with caution** in asthmatics. Reduced dosages have been recommended in patients with renal and hepatic dysfunction. Opatvar **should not be used** to treat contact lens–related irritation. Soft contact lens users should wait at least 10 min after dose instillation before they insert their lenses.



Continued

AZATHIOPRINE *continued*

Drowsiness may occur despite the nasal route of administration (**avoid** concurrent use of alcohol or CNS depressants). Bitter taste, nausea, nasal burning, pharyngitis, weight gain, fatigue, nasal sores, and epistaxis may also occur with nasal route. Eye burning and stinging have been reported in about 30% of patients receiving the ophthalmic dosage form.

**AZITHROMYCIN**

Zithromax, Zithromax TRI-PAK, Zithromax Z-PAK, Zmax (extended-release oral suspension), Azasite, and generics

**Antibiotic, macrolide**



Yes



Yes



2



B

**Tablets:** 250, 500, 600 mg

**TRI-PAK:** 500 mg (3s as unit dose pack)

**Z-PAK:** 250 mg (6s as unit dose pack)

**Oral suspension:** 100 mg/5 mL (15 mL), 200 mg/5 mL (15, 22.5, 30 mL)

**Oral Powder (Sachet):** 1 g (3s, 10s)

**Extended-release oral suspension (microspheres):**

**Zmax:** 2 g reconstituted with 60 mL of water

**Injection:** 500 mg; contains 9.92 mEq Na/1 g drug

**Ophthalmic solution (Azasite):** 1% (2.5 mL)

**Infant and child:****Otitis media (≥6 mo):**

**5-day regimen:** 10 mg/kg PO on day 1 (**max. dose:** 500 mg), followed by 5 mg/kg/24 hr PO once daily (**max. dose:** 250 mg/24 hr) on days 2–5

**3-day regimen:** 10 mg/kg/24 hr PO once daily × 3 days (**max. dose:** 500 mg/24 hr)

**1-day regimen:** 30 mg/kg/24 hr PO × 1 (**max. dose:** 1500 mg/24 hr)

**Community-acquired pneumonia (≥6 mo):**

**Tablet or oral suspension:** Use otitis media 5-day regimen.

**Extended-release oral suspension (Zmax):** 60 mg/kg (**max. dose:** 1500 mg) PO × 1.

**Pharyngitis/tonsillitis (2–15 yr):** 12 mg/kg/24 hr PO once daily × 5 days (**max. dose:** 500 mg/24 hr)

**Acute sinusitis (≥6 mo):** 10 mg/kg/dose (**max. dose:** 500 mg) PO once daily × 3 days

**Pertussis:**

**Infant < 6 mo:** 10 mg/kg/dose PO once daily × 5 days

**≥6 mo:** 10 mg/kg/dose (**max. dose:** 500 mg) PO × 1, followed by 5 mg/kg/ (**max. dose:** 250 mg) PO once daily on days 2–5

**Mycobacterium avium complex in HIV (see [www.aidsinfo.nih.gov/guidelines](http://www.aidsinfo.nih.gov/guidelines) for most current recommendations):**

**Prophylaxis for first episode:** 20 mg/kg/dose PO Q7 days (**max. dose:** 1200 mg/dose); alternatively, 5 mg/kg/24 hr PO once daily (**max. dose:** 250 mg/dose) with or without rifabutin

**Prophylaxis for recurrence:** 5 mg/kg/24 hr PO once daily (**max. dose:** 250 mg/dose), plus ethambutol 15 mg/kg/24 hr (**max. dose:** 900 mg/24 hr) PO once daily with or without rifabutin 5 mg/kg/24 hr (**max. dose:** 300 mg/24 hr)

**Treatment:** 10–12 mg/kg/24 hr PO once daily (**max. dose:** 500 mg/24 hr) × 1 month or longer, plus ethambutol 15–25 mg/kg/24 hr (**max. dose:** 1 g/24 hr) PO once daily with or without rifabutin 10–20 mg/kg/24 hr (**max. dose:** 300 mg/24 hr)

**Endocarditis prophylaxis:** 15 mg/kg/dose (**max. dose:** 500 mg) PO × 1, 30–60 min before procedure

**Anti-inflammatory agent in cystic fibrosis:**

**25–39 kg:** 250 mg PO every Monday, Wednesday, and Friday

**≥40 kg:** 500 mg PO every Monday, Wednesday, and Friday



AZITHROMYCIN *continued***Adolescent and adult:**

**Pharyngitis, tonsillitis, skin, and soft-tissue infection:** 500 mg PO on day 1, then 250 mg/24 hr PO on days 2–5

**Mild/moderate bacterial COPD exacerbation:** Above 5-day dosing regimen **OR** 500 mg PO once daily  $\times$  3 days

**Community-acquired pneumonia:**

**Tablets:** 500 mg PO on day 1, then 250 mg/24 hr PO on days 2–5

**Extended-release oral suspension (Zmax):** Single dose of 2 g PO

**IV and tablet regimen:** 500 mg IV once daily  $\times$  2 days, followed by 500 mg PO once daily to complete a 7–10 day regimen (IV and PO)

**Sinusitis:**

**Tablets:** 500 mg PO once daily  $\times$  3 days

**Extended-release oral suspension (Zmax):** Single dose of 2 g PO

**Uncomplicated chlamydial cervicitis or urethritis:** Single dose of 1 g PO

**Gonococcal cervicitis or urethritis:** Single 2-g dose PO

**Acute PID (chlamydia):** 500 mg IV once daily  $\times$  1–2 days, followed by 250 mg PO once daily to complete a 7-day regimen (IV and PO).

**Mycobacterium avium complex in HIV** (see [www.aidsinfo.nih.gov/guidelines](http://www.aidsinfo.nih.gov/guidelines) for most recent recommendations):

**Prophylaxis for first episode:** 1200 mg PO Q7 days, with or without rifabutin 300 mg PO once daily

**Prophylaxis for recurrence:** 500 mg PO once daily, plus ethambutol 15 mg/kg/dose PO once daily, with or without rifabutin 300 mg PO once daily

**Treatment:** 500–600 mg PO once daily, with ethambutol 15 mg/kg/dose PO once daily, with or without rifabutin 300 mg PO once daily

**Endocarditis prophylaxis:** 500 mg PO  $\times$  1, 30–60 min before procedure

**Anti-inflammatory agent in cystic fibrosis:** Use same dosing as in children.

**Ophthalmic:**

**$\geq 1$  yr and adult:** Instill 1 drop into affected eye(s) BID (8–12 hr apart)  $\times$  2 days, followed by 1 drop once daily for the next 5 days.

**Contraindicated** in hypersensitivity to macrolides and history of cholestatic jaundice/hepatic dysfunction associated with prior use. **Use with caution** in impaired hepatic function, GFR  $<$  10 mL/min (limited data), hypokalemia, hypomagnesemia, bradycardia, arrhythmias, prolonged QT intervals, and receiving medications that can cause the aforementioned conditions of caution. Can cause increase in hepatic enzymes, cholestatic jaundice, GI discomfort, and pain at injection site (IV use). Compared with other macrolides, less risk for drug interactions. Nelfinavir may increase azithromycin levels; monitor for liver enzyme abnormalities and hearing impairment. Vomiting, diarrhea, and nausea have been reported at higher frequency in otitis media with 1-day dosing regimen. Exacerbations of myasthenia gravis/syndrome have been reported. CNS penetration is poor.

Aluminum- and magnesium-containing antacids decrease absorption. Tablet and oral suspension dosage forms may be administered with or without food. Extended-release oral suspension should be taken on an empty stomach (at least 1 hr before or 2 hr after a meal). Intravenous administration is over 1–3 hr; **do not** give as a bolus or IM injection.

**Ophthalmic use:** **Do not** wear contact lenses. Eye irritation is the most common side effect.





**AZTREONAM**

Azactam, Cayston

**Antibiotic, monobactam**

No



Yes



1



B

**Injection:** 1, 2 g**Frozen injection:** 1 g/50 mL 3.4% dextrose, 2 g/50 mL 1.4% dextrose (iso-osmotic solutions)Each 1 g drug contains  $\approx$  780 mg L-arginine**Nebulizer solution (Cayston):** 75 mg powder to be reconstituted with the supplied diluent of 1 mL 0.17% sodium chloride (28-day course kit contains 84 sterile vials of Cayston and 88 ampules of diluent)**Neonate:****30 mg/kg/dose:**

&lt;1.2 kg and 0–4 wk age: Q12 hr IV/IM

1.2–2 kg and 0–7 days: Q12 hr IV/IM

1.2–2 kg and &gt;7 days: Q8 hr IV/IM

&gt;2 kg and 0–7 days: Q8 hr IV/IM

&gt;2 kg and &gt;7 days: Q6 hr IV/IM

**Child:** 90–120 mg/kg/24 hr  $\div$  Q6–8 hr IV/IM**Cystic fibrosis:** 150–200 mg/kg/24 hr  $\div$  Q6–8 hr IV/IM**Adult:****Moderate infections:** 1–2 g/dose Q8–12 hr IV/IM**Severe infections:** 2 g/dose Q6–8 hr IV/IM**Max. dose:** 8 g/24 hr**Inhalation:****Cystic fibrosis prophylaxis therapy:** **$\geq$  7 yr and adult:** 75 mg TID (minimum 4 hr between doses) administered in repeated cycles of 28 days on drug, followed by 28 days off drug. Administer each dose with the Altera Nebulizer System.

Typically indicated in multidrug-resistant aerobic gram-negative infections when  $\beta$ -lactam therapy is contraindicated. Well-absorbed IM. **Use with caution** in arginase deficiency. Low cross-allergenicity between aztreonam and other  $\beta$ -lactams. Adverse reactions: thrombophlebitis, eosinophilia, leukopenia, neutropenia, thrombocytopenia, elevation of liver enzymes, hypotension, seizures, and confusion. Good CNS penetration. Probenecid and furosemide increase aztreonam levels. **Adjust dose in renal failure (see Chapter 31).**

**INHALATIONAL USE:** Cough, nasal congestion, wheezing, pharyngolaryngeal pain, pyrexia, chest discomfort, abdominal pain and vomiting may occur. Bronchospasm has been reported. Use the following order of administration: bronchodilator first, chest physiotherapy, other inhaled medications (if indicated), and aztreonam last.

**BACITRACIN  $\pm$  POLYMYXIN B**

Bacitracin: AK-Tracin Ophthalmic, Baciguent Topical, and others  
 Bacitracin plus polymyxin B: AK-Poly-Bac Ophthalmic, Polysporin Ophthalmic, Polysporin Topical, and others

**Antibiotic, topical**

No



No



?



C

**BACITRACIN:**

Ophthalmic ointment: 500 units/g (3.5 g)

Topical ointment (OTC): 500 units/g (15, 30 g)

BACITRACIN ± POLYMYXIN B *continued***BACITRACIN IN COMBINATION WITH POLYMYXIN B:**

Ophthalmic ointment: 500 units bacitracin + 10,000 units polymyxin B/g (3.5 g)

Topical ointment: 500 units bacitracin + 10,000 units polymyxin B/g (15, 30 g)

**BACITRACIN****Child and adult:****Topical:** Apply to affected area 1–5 times/24 hr.**Ophthalmic:** Apply 0.25- to 0.5-inch ribbon into conjunctival sac of infected eye(s) Q3–12 hr; frequency depends on severity of infection. Administer Q3–4 hr × 7–10 days for mild/moderate infections.**BACITRACIN + POLYMYXIN B****Child and adult:****Topical:** Apply ointment or powder to affected area once daily to TID.**Ophthalmic:** Apply 0.25–0.5 inch ribbon into conjunctival sac of infected eye(s) Q3–12 hr; frequency depends on severity of infection. Administer Q3–4 hr × 7–10 days for mild/moderate infections.

Hypersensitivity reactions to bacitracin and/or polymyxin B can occur. **Do not use** topical ointment for eyes. Side effects may include rash, itching, burning, and edema. Ophthalmic dosage form may cause temporary blurred vision and retard corneal healing. For neomycin-containing products, see Neomycin/Polymyxin B ± Bacitracin.

**BACLOFEN**

Lioresal, Gablofen, Kemstro, and others

**Centrally acting skeletal muscle relaxant**

No



Yes



2



C

**Tabs:** 10, 20 mg**Disintegrating oral tabs (Kemstro):** 10, 20 mg; contains phenylalanine**Oral suspension:** 5, 10 mg/mL **Intrathecal injection (Lioresal, Gablofen):** 50 mcg/mL (1 mL), 0.5 mg/mL (20 mL), 2 mg/mL (5 mL); preservative free

**Oral: Dosage increments, if tolerated, are made at 3-day intervals until desired effect or max. dose is achieved.** Initiate first dosage level at QHS, followed by Q12 hr and then Q8 hr. Dosage increments are made by first increasing the QHS dosage, followed by the morning dosage and then the remaining midday dosage.

**Child (PO, see remarks):**<20 kg: Start at 2.5 mg QHS, increase in 2.5 mg increments if needed up to recommended **max.** dose below.≥20–50 kg: Start at 5 mg QHS, increase in 5 mg increments if needed up to recommended **max.** dose below.>50 kg: Start at 10 mg QHS, increase in 10 mg increments if needed up to recommended **max.** dose below.**Recommended max. PO dose:**

&lt;8 yr: 60 mg/24 hr

8–16 yr: 80 mg/24 hr

&gt;16 yr: 120 mg/24 hr

**Adult (PO):**

Start at 5 mg TID, increase in 5-mg increments if needed up to a maximum of 80 mg/24 hr.

**Intrathecal continuous infusion maintenance therapy (not well established):**

&lt;12 yr: Average dose of 274 mcg/24 hr (range: 24–1199 mcg/24 hr) has been reported.

≥12 yr and adult: Most required 300–800 mcg/24 hr (range: 12–2003 mcg/24 hr with limited experience at doses &gt;1000 mcg/24 hr).

*Continued*

BACLOFEN *continued*

**Avoid** abrupt withdrawal of drug. **Use with caution** in patients with seizure disorders, impaired renal function. About 70%–80% of drug is excreted unchanged in urine. Administer oral doses with food or milk.



**Adverse effects:** Drowsiness, fatigue, nausea, vertigo, psychiatric disturbances, rash, urinary frequency, hypotonia. **Avoid** abrupt withdrawal of intrahecal therapy to prevent potential life-threatening events (rhabdomyolysis, multiple organ-system failure, death). Cases of intrathecal mass at the tip of implanted catheter leading to withdrawal symptoms have been reported. Inadvertent subcutaneous injection may occur with improper access of the reservoir refill septum and may result in overdose.

Usual oral dosage range observed from a single institution retrospective review in 87 patients include:

**2 yr:** 10–20 mg/24 hr to a **maximum** of 40 mg/24 hr

**2–7 yr:** 20–30 mg/24 hr to a **maximum** of 60 mg/24 hr

**≥8 yr:** 30–40 mg/24 hr to a **maximum** of 120 mg/24 hr

**BECLOMETHASONE DIPROPIONATE**

QVAR, Beconase AQ, Qnasl

**Corticosteroid**



Yes



No



2



C

**Inhalation, oral:**

**QVAR:** 40 mcg/inhalation (7.3 g provides 100 inhalations, 8.7 g provides 120 inhalations), 80 mcg/inhalation (4.2 g provides 50 inhalations, 7.3 g provides 100 inhalations, 8.7 g provides 120 inhalations); CFC-free product (HFA)

**Inhalation, nasal:**

**Beconase AQ:** 42 mcg/inhalation (25 g provides 200 metered doses)

**Qnasl:** 80 mcg/inhalation (8.7 g provides 120 metered doses)

**Oral inhalation (QVAR):**

**5–11 yr:** Start at 40 mcg BID; **max. dose:** 80 mcg BID.

**≥12 yr and adult:**

**Corticosteroid naïve:** Start at 40–80 mcg BID; **max. dose:** 320 mcg BID.

**Previous corticosteroid use:** Start at 40–160 mcg BID; **max. dose:** 320 mcg BID.

**Nasal inhalation:****Beconase AQ:**

**6–12 yr:** Start with 1 spray (42 mcg) each nostril BID; may increase to 2 sprays each nostril BID if needed. Once symptoms are controlled, decrease dose to 1 spray each nostril BID.

**>12 yr and adult:** 1–2 spray(s) (42–84 mcg) each nostril BID.

**Qnasl:**

**>12 yr and adult:** 2 sprays (160 mcg) each nostril once daily; **max. dose:** 4 sprays (320 mcg)/24 hr.

Oral inhalation route **not recommended** for children <5 yr, and nasal route **not recommended** for children <6 yr because safety and efficacy are unknown. Dose should be titrated to lowest effective dose. **Avoid** using higher than recommended doses.



Cytochrome P450 (CYP 450) 3A4 inhibitors (e.g., ketoconazole, erythromycin, protease inhibitors) or significant hepatic impairment may increase systemic exposure of beclomethasone.

Monitor for hypothalamic, pituitary, adrenal, or growth suppression and hypercorticism. Instruct patient to rinse mouth and gargle with water after oral inhalation; may cause thrush. Consider using with tube spacers for oral inhalation.

**BENZOYL PEROXIDE**

Benzac AC, Benzac AC Wash 5; Brevoxyl Creamy Wash, Desquam-E 5, Desquam-E 10, NeoBenz Micro, Oxy-5, Oxy-10, and many other products

**Topical acne product**



No



No



?



C

**Liquid wash:** 5% (120, 150, 200 mL), 10% (120, 150, 240 mL)

**Liquid cream wash:** 4% (180 g), 8% (180 g)

**Bar:** 5% [OTC] (113 g), 10% [OTC] (106, 113 g)

**Lotion:** 4% (297 g), 5% [OTC] (30 mL), 6% (170, 340 g), 8% (297 g), 10% [OTC] (30 mL, 85, 170, 340 g)

**Cleanser:** 6% (170, 340 g), 8% (300 g)

**Cleanser/Mask:** [OTC] 3.5% (125 mL)

**Cream:** 5% [OTC] (18 g), 10% [OTC] (30 g)

**Gel:** 2.5% (50 g), 4% (42.5 g), 5% [OTC] (42.5, 60, 90 g), 7% (45 g), 10% (42.5, 60, 90 g)

**NOTE:** Some preparations may contain alcohol and come in combination packs of cleansers and creams at various strengths.

**Combination product with erythromycin (Benzamycin and others):**

**Gel:** 30 mg erythromycin and 50 mg benzoyl peroxide/g (0.8, 23.3, 46 g); some preparations may contain 20% alcohol

**Combination product with clindamycin:**

**Gel:**

**BenzaClin and generics:** 10 mg clindamycin and 50 mg benzoyl peroxide/g (25, 35, 50 g); some preparations may contain methylparaben.

**Duac:** 12 mg clindamycin and 50 mg benzoyl peroxide/g (45 g); Duac CS is packaged with a bottle of soap-free cleanser lotion containing PEG 75, sodium cocoyl isethionate steraryl alcohol, and parabens.

**Acanya:** 12 mg clindamycin and 25 mg benzoyl peroxide/g (50 g).

**Child ≥ 12 yr and adult:**

**Cleansers (liquid wash or bar):** Wet affected area before application. Apply and wash once daily—BID; rinse thoroughly and pat dry. Modify dose frequency or concentration to control amount of drying or peeling.

**Lotion, cream, or gel:** Cleanse skin and apply small amounts over affected areas once daily initially; increase frequency to BID—TID if needed. Modify dose frequency or concentration to control drying or peeling.

**Combination products:**

**Benzamycin, BenzaClin, and generics:** Apply BID (morning and evening) to affected areas after washing and drying skin.

**Duac:** Apply QHS to affected areas after washing and drying skin.

**Acanya:** Apply pea-sized amount once daily.

**Contraindicated** in patients with known history of hypersensitivity to product's components (benzoyl peroxide, clindamycin, or erythromycin). **Avoid** contact with mucous membranes and eyes. May cause skin irritation, stinging, dryness, peeling, erythema, edema, and contact dermatitis. Anaphylaxis has been reported with products containing clindamycin and benzoyl peroxide.

Concurrent use with tretinoin (Retin-A) will increase risk of skin irritation. Products containing clindamycin and erythromycin should not be used in combination.

Any single application resulting in excessive stinging or burning may be removed with mild soap and water. Lotion, cream, and gel dosage forms should be applied to dry skin.



**BENZTROPINE MESYLATE**

Cogentin and various generics

**Anticholinergic agent, drug-induced dystonic reaction  
antidote, antiparkinsonian agent**

No



No



?



?

**Injection:** 1 mg/mL (2 mL)**Tabs:** 0.5, 1, 2 mg**Drug-induced extrapyramidal symptoms (PO/IM/IV):****>3 yr:** 0.02–0.05 mg/kg/dose once daily–BID**Adult:** 1–4 mg/dose once daily–BID**Acute dystonic reaction (phenothiazines) (IM/IV):****Child:** 0.02 mg/kg/dose (**max. dose:** 1 mg)  $\times$  1**Adult:** 1–2 mg/dose  $\times$  1

**Contraindicated** in myasthenia gravis, GI/GU obstruction, untreated narrow-angle glaucoma, and peptic ulcer. Use IV route **only** when PO and IM routes are not feasible. May cause anticholinergic side effects, especially constipation and dry mouth. Drug interactions: potentiation of CNS depressant effects when used with CNS depressants, enhance CNS side effects of amantadine, inhibit response of neuroleptics. This medication has not been formally assigned a pregnancy category by the FDA.

**Onset of action:** 15 min for IV/IM and 1 hr for PO

Oral doses should be administered with food to decrease GI upset.

**BERACTANT**

See Surfactant, pulmonary

**BETAMETHASONE**

Beta-Val, Celestone, Celestone Soluspan, Diprolene, Diprolene AF, Diprosone, Maxivate, and many others

**Corticosteroid**

No



No



3



C

**Betamethasone base (Celestone):****Oral solution:** 0.6 mg/5 mL (120 mL); contains alcohol**Na Phosphate and Acetate (Celestone Soluspan):****Injection suspension:** 6 mg/mL (3 mg/mL Na phosphate + 3 mg/mL betamethasone acetate) (5 mL); may contain benzalkonium chloride and EDTA**Dipropionate (Diprosone, Maxivate, and others):****Topical cream:** 0.05% (15, 45, 50 g)**Topical gel:** 0.05% (15, 50 g)**Topical lotion:** 0.05% (30, 60 mL); may contain 46.8% alcohol and propylene glycol**Topical ointment:** 0.05% (15, 45, 50 g)**Valerate (Beta-Val and others):****Topical cream:** 0.1% (15, 45 g)**Topical foam:** 1.2 mg/g (50, 100 g); may contain 60.4% ethanol, cetyl alcohol, stearyl alcohol, and propylene glycol**Topical lotion:** 0.1% (60 mL); may contain 47.5% isopropyl alcohol**Topical ointment:** 0.1% (15, 45 g)**Dipropionate augmented (Diprolene, Diprolene AF, and others):****Topical cream:** 0.05% (15, 45, 50 g); contains propylene glycol**Topical gel:** 0.05% (15, 50 g); contains propylene glycol

BETAMETHASONE *continued*

**Topical lotion:** 0.05% (30, 60 mL); contains 30% isopropyl alcohol

**Topical ointment:** 0.05% (15, 45, 50 g); contains propylene glycol

*All dosages should be adjusted based on patient response and severity of condition (see remarks).*

**Anti-inflammatory:****Child:**

**Oral:** 0.0175–0.25 mg/kg/24 hr or 0.5–7.5 mg/m<sup>2</sup>/24 hr ÷ Q6–8 hr

**IM:** 0.0175–0.125 mg/kg/24 hr or 0.5–7.5 mg/m<sup>2</sup>/24 hr ÷ Q6–12 hr

**Adolescent and adult:**

**Oral:** 2.4–4.8 mg/24 hr ÷ Q6–12 hr; may range from 0.6–7.2 mg/24 hr depending on disease being treated

**IM:** 0.6–9 mg/24 hr ÷ Q12–24 hr

*Topical (use smallest amount for shortest period of time to avoid adrenal suppression and reassess diagnosis if no improvement is achieved after 2 weeks; see remarks):*

**Valerate and dipropionate forms:**

**Child and adult:** Apply to affected areas once daily–BID

**Dipropionate augmented forms:**

**≥13 yr–adult:** Apply to affected areas once daily–BID

**Max. dose:** 14 days and

**Cream and ointment:** 45 g/week

**Gel:** 50 g/week

**Lotion:** 50 mL/week

**Use with caution** in hypothyroidism, cirrhosis, and ulcerative colitis. See Chapter 10 for relative steroid potencies and doses based on body surface area. Betamethasone is inadequate when used alone for adrenocortical insufficiency because of its minimal mineralocorticoid properties. Like all steroids, may cause hypertension, pseudotumor cerebri, acne, Cushing syndrome, adrenal axis suppression, GI bleeding, hyperglycemia, and osteoporosis.



Na phosphate and acetate injectable suspension recommended for IM, intraarticular, intrasynovial, intralesional, soft-tissue use only; but **not** for IV use. **Topical betamethasone dipropionate augmented (Diprolene and Diprolene AF) is not recommended in children ≤12 yr owing to higher risk for adrenal suppression.**

Injectable dosage form is used in premature labor to stimulate fetal lung maturation.

**BETHANECHOL CHLORIDE**

Urecholine and other brand names

**Cholinergic agent**

No



No




?



C

**Tabs:** 5, 10, 25, 50 mg

**Oral suspension:** 1, 5 mg/mL 

**Child:**

**Abdominal distention/urinary retention:** 0.6 mg/kg/24 hr ÷ Q6–8 hr PO

**Gastroesophageal reflux:** 0.1–0.2 mg/kg/dose 30 min–1 hr before meals and QHS PO;

**max. dose:** 4 doses/24 hr

**Adult:**

**Urinary retention:** 10–50 mg Q6–12 hr PO

**Contraindicated** in asthma, mechanical GI or GU obstruction, peptic ulcer disease, hyperthyroidism, cardiac disease, and seizure disorder. May cause hypotension, nausea (administer doses on an empty stomach to minimize nausea), bronchospasm, salivation,



*Continued*

BETHANECHOL CHLORIDE *continued*

flushing, and abdominal cramps. **Warning:** Severe hypotension may occur when given with ganglionic blockers (e.g., trimethaphan). Atropine is the antidote.

## BICITRA

See Citrate Mixtures

## BISACODYL

Dulcolax, Fleet Laxative, Fleet Bisacodyl, Doxidan, and various other names

**Laxative, stimulant**



No



No



1



B

**Tabs (enteric-coated):** 5 mg

**Suppository:** 10 mg

**Enema (Fleet Bisacodyl):** 10 mg/30 mL (37.5 mL)

**Delayed released tabs (Doxidan):** 5 mg

**Oral:**

**Child (3–12 yr):** 0.3 mg/kg/dose or 5–10 mg × 1 administered 6 hr before desired effect;

**max. dose:** 30 mg/24 hr

**Adolescent and adult (>12 yr):** 5–15 mg × 1 administered 6 hr before desired effect;

**max. dose:** 30 mg/24 hr

**Rectal suppository (as a single dose):**

**<2 yr:** 5 mg

**2–11 yr:** 5–10 mg

**>11 yr and adult:** 10 mg

**Rectal enema (as a single dose):**

**≥12 yr and adult:** 30 mL



**Do not use** in newborn period. Instruct patient/parent that tablets should be swallowed whole, **not** chewed or crushed; **not** to be taken within 1 hr of antacids or milk. May cause abdominal cramps, nausea, vomiting, and rectal irritation. Oral usually effective within 6–10 hr; rectal usually effective within 15–60 min.



Antacids may decrease the effect of bisacodyl and may cause premature release of the delayed-release formulation before reaching large intestine.

## BISMUTH SUBSALICYLATE

Pepto-Bismol, Kaopectate, Kaopectate Extra Strength, Kao-Tin, Stomach Relief, Stomach Relief Max St, Stomach Relief Plus, and many others (see remarks)

**Antidiarrheal, gastrointestinal ulcer agent**



No



Yes



2



C/D

**Liquid [OTC]:**

**Kaopectate, Pepto-Bismol, Stomach Relief, and others:** 262 mg/15 mL (240, 360, 480 mL)

**Kaopectate Extra Strength, Stomach Relief Max St, and Stomach Relief Plus:** 525 mg/15 mL (240, 480 mL)

**Chewable tabs [OTC]:** 262 mg; may contain aspartame

Contains 102 mg salicylate per 262-mg tablet, or 129 mg salicylate per 15 mL of 262-mg/15 mL liquid.

BISMUTH SUBSALICYLATE *continued***Diarrhea:**

**Child:** 100 mg/kg/24 hr ÷ 5 equal doses for 5 days; **max. dose:** 4.19 g/24 hr

**Dosage by age:** Give following dose Q30 min–1 hr PRN up to a **max. dose** of 8 doses/24 hr:

**3–5 yr:** 87.3 mg (½ tablet or 5 mL of 262 mg/15 mL)

**6–8 yr:** 174.7 mg (¾ tablet or 10 mL of 262 mg/15 mL)

**9–11 yr:** 262 mg (1 tablet or 15 mL of 262 mg/15 mL)

**≥12 yr–adult:** 524 mg (2 tablets or 30 mL of 262 mg/15 mL)

**Helicobacter pylori gastric infection** (in combination with ampicillin and metronidazole or with tetracycline and metronidazole for adults; doses not well established for children):

**<10 yr:** 262 mg PO QID × 6 wk

**≥10 yr –adult:** 524 mg PO QID × 6 wk

**Generally not recommended** in children <16 yr with chicken pox or flulike symptoms (risk for Reye syndrome); in combination with other nonsteroidal anti-inflammatory drugs, anticoagulants, or oral antidiabetic agents; or in severe renal failure. **Use with caution** in bleeding disorders, renal dysfunction, gastritis, and gout. May cause darkening of tongue and/or black stools, GI upset, impaction, and decreased platelet aggregation.

Drug combination appears to have antisecretory and antimicrobial effects, with some anti-inflammatory effects. Absorption of bismuth is negligible, whereas roughly 80% of salicylate is absorbed. Decreases absorption of tetracycline. Pregnancy category changes to “D” if used during third trimester.

**DO NOT use** Children's Pepto (calcium carbonate) since it does not contain bismuth subsalicylate.

**Avoid use in renal failure** (see Chapter 31).

**BROMPHENIRAMINE WITH PHENYLEPHRINE**

Dimetapp Children's Cold and Allergy, and many other products

**Antihistamine + decongestant**



No



No



3



C

**Oral syrup (Dimetapp Children's Cold and Allergy) [OTC]:** Brompheniramine 1 mg + phenylephrine 2.5 mg/5 mL (237 mL)

**Chewable tab (Dimetapp Children's Cold and Allergy) [OTC]:** Brompheniramine 1 mg + phenylephrine 2.5 mg

**All doses based on brompheniramine component.**

**2–<6 yr:** 1 mg Q4 hr PO up to a **max. dose** of 6 mg/24 hr

**6–12 yr:** 2 mg Q4 hr PO up to a **max. dose** of 12 mg/24 hr

**≥12 yr:** 4 mg Q4 hr PO up to a **max. dose** of 24 mg/24 hr

**Alternatively, dosing based on specific dosage forms/products. CAUTION:** These products are available in different concentrations.

**Oral, elixir (Dimetapp Children's Cold and Allergy):**

**6–<12 yr:** 10 mL Q4 hr PO up to a **max. dose** of 60 mL/24 hr

**≥12 yr:** 20 mL Q4 hr PO up to a **max. dose** of 120 mL/24 hr

**Oral, chewable tab (Dimetapp Children's Cold and Allergy):**

**6–<12 yr:** Chew 2 tablets Q4 hr PO; **max. dose:** 6 doses/24 hr

**≥12 yr:** Chew 4 tablets Q4 hr PO; **max. dose:** 6 doses/24 hr

**Generally not recommended** for treating URIs for infants. No proven benefit for infants and young children with URIs. Over-the-counter (OTC or nonprescription) use of this product is **not recommended** for children <6 years owing to reports of serious adverse effects (cardiac and respiratory distress, convulsions, and hallucinations) and fatalities (from unintentional overdosages, including combined use of other OTC products containing the same active ingredients).

*Continued*



BROMPHENIRAMINE WITH PHENYLEPHRINE *continued*

**Contraindicated** with use of MAO inhibitors (concurrent use and within 14 days after discontinuing MAO inhibitor). **Use with caution** in narrow-angle glaucoma, bladder neck obstruction, asthma, pyloroduodenal obstruction, symptomatic prostatic hypertrophy, hypertension, coronary artery disease, diabetes mellitus, and thyroid disease. Discontinue use 48 hours before allergy skin testing. May cause drowsiness, fatigue, CNS excitation, xerostomia, blurred vision, and wheezing.

**BUDESONIDE**

Pulmicort Respules, Pulmicort Flexhaler, Rhinocort Aqua Nasal Spray, Entocort EC, Uceris, and generics

**Corticosteroid**

Yes



No



2



B/C

**Nasal spray (Rhinocort Aqua):** 32 mcg/actuation (8.6 g, delivers approx. 120 sprays)

**Nebulized inhalation suspension (Pulmicort Respules and generics):** 0.25 mg/2 mL, 0.5 mg/2 mL (30s)

**Oral inhalation powder:**

**Pulmicort Flexhaler:** 90 mcg/metered dose (165 mg, delivers 60 doses), 180 mcg/metered dose (225 mg, delivers 120 doses); contains lactose

**Enteric-coated caps (Entocort EC and generics):** 3 mg

**Extended-release tabs (Uceris):** 9 mg

**Nebulized inhalation suspension:****Child 1–8 yr:**

**No prior steroid use:** 0.5 mg/24 hr ÷ once daily–BID; **max. dose:** 0.5 mg/24 hr

**Prior inhaled steroid use:** 0.5 mg/24 hr ÷ once daily–BID; **max. dose:** 1 mg/24 hr

**Prior oral steroid use:** 1 mg/24 hr ÷ once daily–BID; **max. dose:** 1 mg/24 hr

**NIH Asthma Guideline 2007 recommendations (divide doses once daily–TID):****Child 0–4 yr:**

**Low dose:** 0.25–0.5 mg/24 hr

**Medium dose:** >0.5–1 mg/24 hr

**High dose:** >1 mg/24 hr

**Child 5–11 yr:**

**Low dose:** 0.5 mg/24 hr

**Medium dose:** 1 mg/24 hr

**High dose:** 2 mg/24 hr

**Oral inhalation:****Pulmicort Flexhaler:**

**Child ≥ 6 yr:** Start at 180 mcg BID; **max. dose:** 720 mcg/24 hr.

**Adult:** Start at 180–360 mcg BID; **max. dose:** 1440 mcg/24 hr.

**Nasal inhalation (≥6 yr and adult):**

**Rhinocort Aqua (initial):** 1 spray in each nostril once daily. Increase dose as needed up to **max. dose.**

**Max. nasal dose:** 6–11 yr: 128 mcg/24 hr (4 sprays/24 hr); ≥12 yr and adult: 256 mcg/24 hr (8 sprays/24 hr)

**Crohn's disease (Encort EC):**

**Child ≥ 6 yr:** Data are limited; following dosages have been reported, but additional studies are warranted.

**Active disease:** 9 mg PO once daily × 7–8 wk

**Maintenance of remission:** 6 mg PO once daily × 3–4 wk

A report in 10- to 19-year-old patients demonstrated higher remission rates with an induction dose of 12 mg PO once daily × 4 wk, followed by 9 mg PO once daily × 3 wk, followed by 6 mg PO once daily × 3 wk.



BUDESONIDE *continued***Adult:**

**Active disease:** 9 mg PO QAM  $\times$  8 wk; if remission is not achieved, a second 8-week course may be given.

**Maintenance of remission:** 6 mg PO once daily for up to 3 mo. If symptom control is maintained at 3 mo, taper dosage to compete cessation. Remission therapy beyond 3 mo has not been shown to provide substantial clinical benefit.

**Ulcerative colitis, induction of remission (Uceris):**

**Adult:** 9 mg PO QAM for up to 8 weeks

Reduce maintenance dose to as low as possible to control symptoms. May cause pharyngitis, cough, epistaxis, nasal irritation, and HPA-axis suppression. Instruct patient to rinse mouth after each use via the oral inhalation route. Nebulized budesonide has been shown effective in mild to moderate croup at doses of 2 mg  $\times$  1. Ref: *N Engl J Med.* 331:285.

Hypersensitivity reactions (including anaphylaxis) have been reported with the inhaled route. Anaphylactic reactions and benign intracranial hypertension have been reported with oral administration.

CYP 450 3A4 inhibitors (e.g., ketoconazole, erythromycin, protease inhibitors) or significant hepatic impairment may increase systemic exposure of budesonide (inhalation and PO routes)

Onset of action for oral inhalation and nebulized suspension is within 1 day and 2–8 days, respectively, with peak effects at 1–2 wk and 4–6 wk, respectively.

For nasal use, onset of action is seen after 1 day, with peak effects after 3–7 days of therapy.

Discontinue therapy if no improvement in nasal symptoms after 3 wk of continuous therapy.

Pregnancy category is “B” for inhalation routes of administration and “C” for oral route. Instruct patient/parent that oral capsule dosage form should be swallowed whole, **not** chewed or crushed.

**BUDESONIDE AND FORMOTEROL**

Symbicort

**Corticosteroid and long-acting  $\beta_2$ -adrenergic agonist**



Yes



No



?



C

**Aerosol inhaler:**

80 mcg budesonide + 4.5 mcg formoterol fumarate dihydrate (6.9 g delivers 60 inhalations, 10.2 g delivers about 120 inhalations)

160 mcg budesonide + 4.5 mcg formoterol fumarate dihydrate (6 g delivers 60 inhalations, 10.2 g delivers about 120 inhalations)

**5–11 yr (NIH Asthma Guideline 2007 recommendations):** 2 inhalations BID of 80 mcg budesonide + 4.5 mcg fomoterol; **max. dose:** 4 inhalations/24 hr

 **$\geq 12$  yr and adult:**

**No prior inhaled steroid use:** Start with 2 inhalations BID of 80 mcg budesonide + 4.5 mcg fomoterol OR 160 mcg budesonide + 4.5 mcg fomoterol, depending on severity.

**Prior low to medium doses of inhaled steroid use:** Start with 2 inhalations BID of 80 mcg budesonide + 4.5 mcg fomoterol.

**Prior medium to high doses of inhaled steroid use:** Start with 2 inhalations BID of 160 mcg budesonide + 4.5 mcg fomoterol.

**Max. dose:** 2 inhalations of 160 mcg budesonide + 4.5 mcg fomoterol BID

See *Budesonide* and *Fomoterol* for remarks. Should only be used for patients not adequately controlled on other asthma-controller medications (e.g., low- to medium-dose inhaled corticosteroids) or whose disease severity requires use of two maintenance therapies. Titrate to lowest effective strength after asthma is adequately controlled. Proper patient education, including dosage administration technique is essential; see patient package insert for detailed instructions. Instruct patient to rinse mouth after each use.

**BUMETANIDE**

Bumex and other generics

*Loop diuretic*

Yes



No



?



C/D

**Tabs:** 0.5, 1, 2 mg**Injection:** 0.25 mg/mL (2, 4, 10 mL); some preparations may contain 1% benzyl alcohol**Neonate and infant (see remarks):** PO/IM/IV**≤6 mo:** 0.01–0.05 mg/kg/dose once daily or every other day**Infant and child:** PO/IM/IV**>6 mo:** 0.015–0.1 mg/kg/dose once daily–BID; **max. dose:** 10 mg/24 hr**Adult:****PO:** 0.5–2 mg/dose once daily–BID**IM/IV:** 0.5–1 mg over 1–2 min. May give additional doses Q2–3 hr PRN**Usual max. dose (PO/IM/IV):** 10 mg/24 hr

Cross-allergenicity may occur in patients allergic to sulfonamides. Dosage reduction may be necessary in patients with hepatic dysfunction. Administer oral doses with food.

Side effects include cramps, dizziness, hypotension, headache, electrolyte losses (hypokalemia, hypocalcemia, hyponatremia, hypochloremia), and encephalopathy. May also lead to metabolic alkalosis. Serious skin reactions (e.g., Stevens-Johnson, TEN) have been reported.

Drug elimination has been reported to be slower in neonates with respiratory disorders compared with neonates without. May displace bilirubin in critically ill neonates. **Maximal** diuretic effect for infants ≤6 mo has been reported at 0.04 mg/kg/dose, with greater efficacy seen at lower dosages.

Pregnancy category changes to “D” if used in pregnancy-induced hypertension.

**BUTORPHANOL**

Stadol and other generics

*Narcotic, analgesic*

Yes



Yes



3



C

**Injection:** 1 mg/mL (1 mL), 2 mg/mL (1, 2, 10 mL)**Nasal solution:** 10 mg/mL (2.5 mL); 1 mg per spray**Child:** 0.03–0.05 mg/kg/dose (**max. dose:** 2 mg/dose) IV Q3–4 hr PRN**Adult:****IV:** 1 mg/dose Q3–4 hr PRN; usual dosage range: 0.5–2 mg Q3–4 hr PRN**IM:** 2 mg/dose Q3–4 hr PRN; usual dosage range: 1–4 mg Q3–4 hr PRN

**Intranasal:** 1 spray (1 mg) in one nostril × 1; an additional 1-mg dose may be given at 1–1.5 hr if needed. This 2-dose sequence may be repeated in 3–4 hr if needed. Alternatively, patient may receive 2 mg initially (1 mg in each nostril) only if they remain recumbent if drowsiness or dizziness occurs; an additional dose may be given 3–4 hr later.

A synthetic mixed agonist/antagonist opioid analgesic. **Contraindicated** in patients hypersensitive to benzethonium chloride. **Use with caution** in hypotension, thyroid dysfunction, renal or hepatic impairment, and concomitant CNS depressants. **Suggested dosage reduction** in renal impairment (IV/IM): 75% of usual dose for GFR 10–50 mL/min and 50% of usual dose for GFR <10 mL/min, with an increase in dosage interval based on duration of clinical effects. A 50% IV/IM dosage reduction with increased dosage interval has been recommended in hepatic dysfunction. Reduced dosage for intranasal administration for both renal and hepatic impairment: initial dose should not exceed 1 mg.

Common side effects include drowsiness, dizziness, insomnia (nasal spray), nausea, vomiting, nasal congestion (nasal spray).

**Onset of action:** 5–10 min (IV); 0.5–1 hr (IM); and within 15 min (intranasal)**Duration:** 3–4 hr (IV/IM) and 4–5 hr (intranasal)

**CAFFEINE CITRATE**

Cafcit and others

**Methylxanthine, respiratory stimulant**

Yes



Yes



2



C

**Injection:** 20 mg/mL (3 mL)**Oral liquid:** 20 mg/mL (3 mL), also available as powder for compounding 10, 20 mg/mL 

20 mg/mL caffeine citrate salt = 10 mg/mL caffeine base

**Doses expressed in mg of caffeine citrate.****Neonatal apnea:****Loading dose:** 20–25 mg/kg IV/PO  $\times$  1**Maintenance dose:** 5–10 mg/kg/dose PO/IV Q24 hr, to begin 24 hr after loading dose**Avoid use** in symptomatic cardiac arrhythmias. **Do not use** caffeine benzoate formulation; it has been associated with kernicterus in neonates. **Use with caution** in impaired renal or hepatic function.**Therapeutic levels:** 5–25 mg/L. Cardiovascular, neurologic, or GI toxicity reported at serum levels >50 mg/L. Recommended serum sampling time: obtain trough level within 30 minutes before a dose. Steady state is typically achieved 3 wk after initiation of therapy. Levels obtained before steady state are useful for preventing toxicity.

For IV administration, give loading dose over 30 min and maintenance dose over 10 min.

**CALCITONIN—SALMON**

Miacalcin, Miacalcin Nasal Spray, Fortical Nasal Spray

**Hypercalcemia antidote, antiosteoporotic**

No



No



?



C

**Injection:** 200 U/mL (2 mL); contains phenol**Nasal spray:** 200 U/metered dose (3.7 mL, provides at least 30 doses); may contain benzyl alcohol**Hypercalcemia (see remarks):****Adult:** Start with 4 U/kg/dose IM/SC Q12 hr; if response is unsatisfactory after 1 or 2 days, increase dose to 8 U/kg/dose Q12 hr. If response remains unsatisfactory after 2 more days, increase to a **max. dose** of 8 U/kg/dose Q6 hr.**Paget disease (see remarks):****Adult:** Start with 100 U IM/SC once daily initially, followed by a usual maintenance dose of 50 U once daily QR 50–100 U Q1–3 days.**Contraindicated** in patients sensitive to salmon protein or gelatin. Because of hypersensitivity risk (e.g., bronchospasm, airway swelling, anaphylaxis), skin test is recommended before starting IM/SC therapy. For skin test, prepare a 10 U/mL dilution with normal saline, administer 0.1 mL intradermally, and observe for 15 min for wheal or significant erythema. Tachyphylaxis has been reported after 2–3 days of use for treatment of hypercalcemia of malignancy.

Nausea, abdominal pain, diarrhea, flushing, and inflammation at injection site has been reported with IM/SC route of administration.

Intranasal use currently indicated for postmenopausal osteoporosis in adults. Nasal irritation (alternate nostrils to reduce risk), rhinitis, epistaxis may occur with intranasal product.

Tremors has been reported with both intranasal and injectable routes of administration.

If injection volume exceeds 2 mL, use IM route and multiple sites of injection.

**CALCITRIOL**

1,25-dihydroxycholecalciferol, Rocaltrol, Calcijex, and generics

**Active form vitamin D, fat soluble**

No



No



2



C/D

**Caps:** 0.25, 0.5 mcg; may contain parabens**Oral solution:** 1 mcg/mL (15 mL)**Injection:** (Calcijex and others) 1 mcg/mL (1 mL); contains EDTA**Hypoparathyroidism (evaluate dosage at 2–4 wk intervals):****Child > 1 yr and adult:** initial dose of 0.25 mcg/dose PO once daily. May increase daily dosage by 0.25 mcg at 2- to 4-wk intervals. Usual maintenance dosage as follows:

&lt;1 yr: 0.04–0.08 mcg/kg/dose PO once daily

1–5 yr: 0.25–0.75 mcg/dose PO once daily

&gt;6 yr and adult: 0.5–2 mcg/dose PO once daily

**Renal failure:** See National Kidney Foundation guidelines at <http://www.kidney.org/professionals/kdoqi/guidelinespedbone/guide9.htm>.

Most potent vitamin D metabolite available. Should not be used to treat 25-OH vitamin D deficiency; use cholecalciferol or ergocalciferol. Monitor serum calcium, phosphorus, and PTH in dialysis patients. **Avoid** concomitant use of Mg<sup>2+</sup>-containing antacids. IV dosing applies if patient undergoing hemodialysis.

**Contraindicated** in patients with hypercalcemia, vitamin D toxicity. Side effects include weakness, headache, vomiting, constipation, hypotonia, polydipsia, polyuria, myalgia, metastatic calcification, etc. Allergic reactions, including anaphylaxis, have been reported.

Pregnancy category changes to D if used in doses above the recommended daily allowance.

**CALCIUM ACETATE**

PhosLo, Calphron, Eliphos, Phoslyra, and generics;

25% elemental Ca

**Calcium supplement, phosphorous-lowering agent**

No



Yes



2



C

**Tabs:** 667 mg (169 mg elemental Ca)**Capsules:** 667 mg (169 mg elemental Ca)**Oral solution (Phoslyra):** 667 mg/5 mL (473 mL) (169 mg elemental Ca per 5 mL); contains methylparabens and propylene glycol

Each 1 g of salt contains 12.7 mEq (250 mg) elemental Ca.

**Doses expressed in mg of calcium acetate.****Hyperphosphatemia:****Adult:** Start with 1334 mg PO with each meal. Dosage may be increased gradually to bring serum phosphorous levels below 6 mg/dL, so long as hypercalcemia does not occur. Most patients require 2001–2668 mg PO with each meal.

**Contraindicated** in ventricular fibrillation. **Use with caution** in renal impairment; hypercalcemia may develop in end-stage renal failure. Nausea and hypercalcemia may occur.

About 40% of dose is systemically absorbed under fasting conditions and up to 30% in nonfasting conditions. May reduce absorption of tetracyclines, iron, and effectiveness of polystyrene sulfonate. May potentiate effects of digoxin.

Administer with meals and plenty of fluids for use as a phosphorus-lowering agent. Calcium is excreted in breast milk and is not expected to harm the infant, provided maternal serum calcium is appropriately monitored.

**CALCIUM CARBONATE**

Tums, Os-Cal, Children's Pepto, and many others;  
40% elemental Ca

**Calcium supplement, antacid**



No



Yes



2



C

**Tab, chewable [OTC]:** 400, 500, 600, 750, 1000, 1250 mg

**Children's Pepto [OTC]:** 400 mg

**Tab [OTC]:** 500, 600, 650, 1250, 1500 mg

**Oral suspension [OTC]:** 1250 mg/5 mL

**Caps [OTC]:** 200, 364, 1250 mg

**Powder [OTC]:** 800 mg/2 g (480 g)

Each 1 g of salt contains 20 mEq elemental Ca (400 mg elemental Ca).

**Hypocalcemia (Doses expressed in mg of elemental calcium. To convert to mg of salt, divide elemental dose by 0.4):**

**Neonate:** 50–150 mg/kg/24 hr ÷ Q4–6 hr PO; **max. dose** 1 g/24 hr

**Child:** 45–65 mg/kg/24 hr PO ÷ QID

**Adult:** 1–2 g/24 hr PO ÷ TID–QID

**Antacid (Doses expressed in mg of calcium carbonate):**

**2–5 yr:** 400 mg PO as symptoms occur; **max. dose** 1200 mg/24 hr

**>6–11 yr:** 800 mg PO as symptoms occur; **max. dose** 2400 mg/24 hr

**>11 yr and adult:** 1000–3000 mg PO as symptoms occur; **max. dose** 7500 mg/24 hr

See *Calcium Acetate* for **contraindications, precautions** and drug interactions. Side effects:

constipation, hypercalcemia, hypophosphatemia, hypomagnesemia, nausea, vomiting, headache, and confusion. Some products may contain trace amounts of sodium. Administer with plenty of fluids. For use as a phosphorus-lowering agent, administer with meals. Calcium is excreted in breast milk and is not expected to harm the infant, provided maternal serum calcium is appropriately monitored.

**CALCIUM CHLORIDE**

Various generics; 27% elemental Ca

**Calcium supplement**



No



Yes



2



C

**Injection:** 100 mg/mL (10%) (1.36 mEq Ca/mL); 1 g of salt contains 13.6 mEq (273 mg) elemental Ca  
Each 1 g of salt contains 13.5 mEq (270 mg) elemental Ca.

**Doses expressed in mg of CaCl.**

**Cardiac arrest or calcium channel blocker toxicity:**

**Infant/child:** 20 mg/kg/dose IV Q10 min PRN; if effective, an infusion of 20–50 mg/kg/hr may be used

**Adult:** 500–1000 mg/dose IV Q10 min PRN OR 2–4 mg/kg/dose Q10 min PRN

**MAXIMUM IV ADMINISTRATION RATES:**

**IV push:** Do not exceed 100 mg/min (over 10–20 sec in cardiac arrest).

**IV infusion:** Do not exceed 45–90 mg/kg/hr with a **max. concentration** of 20 mg/mL.

**Contraindicated** in ventricular fibrillation. **Not recommended** for asystole and electromechanical dissociation. **Use with caution** in renal impairment; hypercalcemia may develop in end-stage renal failure. May potentiate effects of digoxin.

**Use IV with extreme caution.** Extravasation may lead to necrosis. Hyaluronidase may be helpful for extravasation. Central-line administration is preferred IV route of administration. **Do not use** scalp veins. **Do not administer via IM or SC routes.**

Rapid IV infusion associated with bradycardia, hypotension, and peripheral vasodilation. May cause hyperchloremic acidosis.

Calcium is excreted in breast milk and is not expected to harm the infant, provided maternal serum calcium is appropriately monitored.

**CALCIUM CITRATE**

Cal-Citrate, Citracal, and generics; 21% elemental Ca

**Calcium supplement**

No



Yes



2



C

**Tabs [OTC]:** 950 mg (200 mg elemental), 1150 mg calcium citrate (250 mg elemental Ca)**Caps [OTC]:****As elemental calcium:** 180, 225 mg**Granules [OTC]:****As elemental calcium:** 760 mg/teaspoonful or 3.5 g of granules (480 g)

Each 1 g of salt contains 10.6 mEq (211 mg) elemental Ca.

Some products may be combined with vitamin D.

**Doses expressed as mg of elemental calcium. To convert to mg of salt, divide elemental dose by 0.21.****Hypocalcemia:****Neonate:** 50–150 mg/kg/24 hr ÷ Q4–6 hr PO; **max. dose** 1 g/24 hr**Child:** 45–65 mg/kg/24 hr PO ÷ QID**Adult:** 1–2 g/24 hr PO ÷ TID–QIDSee *Calcium Acetate* for **contraindications, precautions**, and drug interactions. Side effects: constipation, hypercalcemia, hypophosphatemia, hypomagnesemia, nausea, vomiting, headache, and confusion.

Administer with meals for use as a phosphorus-lowering agent or with use of the granule dosage form.

For hypocalcemia, do not administer with or before meals/food, and take plenty of fluids.

Calcium is excreted in breast milk and is not expected to harm the infant, provided maternal serum calcium is appropriately monitored.

**CALCIUM GLUBIONATE**

Calcionate, Calciqid, and generics; 6.4% elemental Ca

**Calcium supplement**

No



Yes



2



C

**Syrup [OTC]:** 1.8 g/5 mL (480 mL) (1.2 mEq Ca/mL)

Each 1 g of salt contains 3.2 mEq (64 mg) elemental Ca.

**Doses expressed in mg calcium glubionate.****Hypocalcemia:****Neonate:** 1200 mg/kg/24 hr PO ÷ Q4–6 hr**Infant/child:** 600–2000 mg/kg/24 hr PO ÷ QID; **max. dose** 9 g/24 hr**Adult:** 6–18 g/24 hr PO ÷ QIDSee *Calcium Acetate* for **contraindications, precautions**, and drug interactions. Side effects include GI irritation, dizziness, and headache. High osmotic load of syrup (20% sucrose) may cause diarrhea.

Best absorbed when given before meals. Absorption inhibited by high phosphate load.

Calcium is excreted in breast milk and is not expected to harm the infant, provided maternal serum calcium is appropriately monitored.

**CALCIUM GLUCONATE**

Cal-Glu and various generics; 9% elemental Ca

**Calcium supplement**

No



Yes



2



C

**Tabs [OTC]:** 50, 500, 648 mg**Caps (Cal-Glu) [OTC]:** 500 mg**Injection:** 100 mg/mL (10%) (0.45 mEq Ca<sup>2+</sup>/mL)

Each 1 g of salt contains 4.5 mEq (90 mg) elemental Ca

**Doses expressed in mg calcium gluconate.****Maintenance/hypocalcemia:****Neonate:** IV: 200–800 mg/kg/24 hr ÷ Q6 hr**Infant:****IV:** 200–500 mg/kg/24 hr ÷ Q6 hr**PO:** 400–800 mg/kg/24 hr ÷ Q6 hr**Child:** 200–500 mg/kg/24 hr IV or PO ÷ Q6 hr**Adult:** 0.5–8 g/24 hr IV or PO ÷ Q6 hr**For cardiac arrest:****Infant and child:** 100 mg/kg/dose IV Q10 min**Adult:** 1.5–3 g/dose IV Q10 min**Max. dose:** 3 g/dose**For tetany:****Neonate, infant, child:** 100–200 mg/kg dose IV over 5–10 min, repeat dose 6 hr later if needed;**max. dose** 500 mg/kg/24 hr**Adult:** 0.5–2 g IV over 10–30 min; repeat dose 6 hr later if needed**MAXIMUM IV ADMINISTRATION RATES:****IV push:** Do not exceed 100 mg/min (over 10–20 sec in cardiac arrest)**IV infusion:** Do not exceed 200 mg/min with a **maximum** concentration of 50 mg/mL

**Contraindicated** in ventricular fibrillation. **Use with caution** in renal impairment; hypercalcemia may develop in end-stage renal failure. **Avoid** peripheral infusion; extravasation may cause tissue necrosis. IV infusion associated with hypotension and bradycardia; also associated with arrhythmias in digitalized patients. May reduce absorption of tetracycline, iron, and effectiveness of polystyrene sulfonate with oral route of administration.

May precipitate when used with bicarbonate. **Do not use scalp veins. Do not administer IM or SC.**

Calcium is excreted in breast milk and is not expected to harm the infant, provided maternal serum calcium is appropriately monitored.

**CALCIUM LACTATE**

Cal-Lac and various generics; 13% elemental Ca

**Calcium supplement**

No



Yes



2



C

**Tabs [OTC]:** 100, 325, 650 mg**Caps (Cal-Lac) [OTC]:** 500 mg

Each 1 g salt contains 6.5 mEq (130 mg) elemental Ca

**Doses expressed in mg of calcium lactate.****Hypocalcemia:****Neonate/Infant:** 400–500 mg/kg/24 hr PO ÷ Q4–6 hr**Child:** 500 mg/kg/24 hr PO ÷ Q6–8 hr**Adult:** 1.5–3 g PO Q8 hr**Max. dose:** 9 g/24 hr

Continued



CALCIUM LACTATE *continued*

See *Calcium Acetate* for **contraindications**, **precautions**, and drug interactions. May cause constipation, headache, and hypercalcemia.

Give with or following meals and with plenty of fluids. **Do not** dissolve tablets in milk.

Calcium is excreted in breast milk and is not expected to harm the infant, provided maternal serum calcium is appropriately monitored.

**CALCIUM PHOSPHATE, TRIBASIC**

Posture-D; 39% elemental Ca

**Calcium supplement**



No



Yes




2



C

**Tabs [OTC]:** 600 mg elemental calcium and 280 mg phosphorus; with 500 IU vitamin D and 50 mg magnesium

**Oral suspension:** 10 mg elemental calcium/1 mL 

**NOTE:** Pharmacy may crush tablets into a powder to enhance drug delivery for children unable to swallow tablets and to accommodate smaller doses.

**Doses expressed as mg of elemental calcium.****Hypocalcemia:**

**Neonate:** 20–80 mg/kg/24 hr ÷ Q4–6 hr PO; **max. dose** 1 g/24 hr

**Child:** 45–65 mg/kg/24 hr PO ÷ Q6 hr

**Adult:** 1–2 g/24 hr PO ÷ Q6–8 hr



**Contraindicated** in ventricular fibrillation. **Use with caution** in renal impairment; hypercalcemia may develop in end-stage renal failure (avoid use in dialysis with hypercalcemia), history of kidney stones, and parathyroid disorders. May cause constipation, GI disturbances, and hypercalcemia. See *Calcium Acetate* for drug interactions.

Give with or following meals and with plenty of fluids. Keep in mind the amounts of vitamin D and magnesium your respective dosage may provide.

Calcium is excreted in breast milk and is not expected to harm the infant, provided maternal serum calcium is appropriately monitored.

**CALFACTANT**

See Surfactant, pulmonary

**CAPTOPRIL**

Capoten and various generics

**Angiotensin-converting enzyme inhibitor, antihypertensive**



No



Yes




2



D

**Tabs:** 12.5, 25, 50, 100 mg

**Oral suspension:** 0.75, 1 mg/mL 

**Neonate:** 0.01–0.05 mg/kg/dose PO Q8–12 hr.

**Infant < 6 mo:** Initially 0.01–0.5 mg/kg/dose PO BID–TID; titrate upward if needed;

**max. dose:** 6 mg/kg/24 hr.

**Child:** Initially 0.3–0.5 mg/kg/dose PO BID–TID; titrate upward if needed; **max. dose** 6 mg/kg/24 hr up to 450 mg/24 hr.

**Adolescent and adult:** Initially 12.5–25 mg/dose PO BID–TID; increase weekly if necessary by 25 mg/dose to **max. dose** of 450 mg/24 hr. Usual dosage range: 25–100 mg/24 hr ÷ BID.



CAPTOPRIL *continued*

Onset within 15–30 min of administration. Peak effect within 1–2 hr. **Adjust dose with renal failure (see Chapter 31).** Should be administered on an empty stomach 1 hr before or 2 hr after meals. Titrate to minimal effective dose. Lower doses should be used in patients with sodium and water depletion due to diuretic therapy.

**Use with caution** in collagen vascular disease and concomitant potassium-sparing diuretics. **Avoid use** with dialysis with high-flux membranes; anaphylactoid reactions have been reported. May cause rash, proteinuria, neutropenia, cough, angioedema (head, neck, and intestinal), hyperkalemia, hypotension, or diminution of taste perception (with long-term use). Known to decrease aldosterone and increase renin production. Do not coadminister with angiotensin receptor blockers or aliskiren, because use has been associated with increased risks for hypotension, hyperkalemia, and acute renal failure. Captopril is a CYP P450 2D6 substrate.

Captopril should be discontinued as soon as possible when pregnancy is detected.

**CARBAMAZEPINE**

Epitol, Tegretol, Tegretol-XR, Carbatrol, and various generics

**Anticonvulsant**



Yes



Yes



2



D

**Tabs:** 200 mg

**Chewable tabs:** 100 mg

**Extended-release tabs (Tegretol-XR and generics):** 100, 200, 400 mg

**Extended-release caps (Carbatrol and generics):** 100, 200, 300 mg

**Oral suspension:** 100 mg/5 mL (10, 450 mL); may contain propylene glycol

**See remarks regarding dosing intervals for specific dosage forms:**

**<6 yr:**

**Initial:** 10–20 mg/kg/24 hr PO ÷ BID–TID (QID for suspension)

**Increment:** Q5–7 days up to **max. dose** of 35 mg/kg/24 hr PO

**6–12 yr:**

**Initial:** 10 mg/kg/24 hr PO ÷ BID up to **max. dose** 100 mg/dose BID

**Increment:** 100 mg/24 hr at 1-wk intervals (÷TID–QID) until desired response is obtained

**Maintenance:** 20–30 mg/kg/24 hr PO ÷ BID–QID; usual maintenance dose is 400–800 mg/24 hr; **max. dose** 1000 mg/24 hr

**>12 yr and adult:**

**Initial:** 200 mg PO BID

**Increment:** 200 mg/24 hr at 1-wk intervals (÷BID–QID) until desired response is obtained

**Maintenance:** 800–1200 mg/24 hr PO ÷ BID–QID

**Max. dose:**

**Child 12–15 yr:** 1000 mg/24 hr

**Child > 15 yr:** 1200 mg/24 hr

**Adult:** 1.6–2.4 g/24 hr

**Contraindicated** for patients taking MAO inhibitors or who are sensitive to tricyclic antidepressants. Should **not** be used in combination with clozapine, owing to increased risk for bone marrow suppression and agranulocytosis. Increased risk for severe dermatologic reactions (e.g., SJS and TEN) has been associated with the HLA-B\*1502 (prevalent among persons of Asian descent) and HLA-A\*3101 (prevalent among Japanese, Native American, Southern Indian, and some Arabic ancestry) alleles.

Erythromycin, diltiazem, verapamil, cefixime, cimetidine, itraconazole, aprepitant, and INH may increase serum levels. Carbamazepine may decrease activity of warfarin, doxycycline, oral

*Continued*

CARBAMAZEPINE *continued*

contraceptives, cyclosporine, theophylline, phenytoin, benzodiazepines, ethosuximide, and valproic acid. Carbamazepine is a CYP 450 3A3/4 substrate and inducer of CYP 450 1A2, 2C, and 3A3/4. The enzyme-inducing effects may increase effects/toxicity of cyclophosphamide.

*Suggested dosing intervals for specific dosage forms:*

Extended-release tabs or caps, BID; chewable and immediate-release tabs, BID–TID; suspension, QID.

Doses may be administered with food. **Do not** crush or chew extended-release dosage forms. Shake bottle thoroughly before dispensing oral suspension dosage form, and **do not** administer simultaneously with other liquid medicines or diluents.

Drug metabolism typically increases after the first month of therapy initiation, owing to hepatic autoinduction.

Therapeutic blood levels: 4–12 mg/L. Recommended serum sampling time: Obtain trough level within 30 min before an oral dose. Steady state is typically achieved 1 month after initiation of therapy (after enzymatic autoinduction). Levels obtained before steady state are useful for preventing toxicity. Blood levels of 7–10 mg/L have been recommended for bipolar disorders.

Side effects include sedation, dizziness, diplopia, aplastic anemia, neutropenia, urinary retention, nausea, SIADH, and Stevens-Johnson syndrome. Suicidal behavior or ideation and onychomadesis have been reported. Pretreatment CBCs and LFTs are suggested. Patient should be monitored for hematologic and hepatic toxicity. **Adjust dose in renal impairment (see Chapter 31).**

See Chapter 2 for management of ingestions.

**CARBAMIDE PEROXIDE**

Debrox, Murine Ear, Auro Ear Drops, Thera-Ear Gly-Oxide, and generics

***Cerumenolytic, topical oral analgesic***



No



No



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**Otic solution [OTC]:** 6.5% (15, 30 mL); may contain propylene glycol or alcohol

**Oral liquid [OTC]:** 10% (Gly-Oxide) (15, 60 mL)

***Cerumenolytic:***

**<12 yr:** Tilt head sideways and instill 1–5 drops (according to patient size) into affected ear; retain drops in ear for several minutes. Remove wax by gently flushing ear with warm water, using a soft rubber bulb ear syringe. Dose may be repeated BID PRN for up to 4 days.

**≥12 yr:** Following the same instructions from above, instill 5–10 drops into affected ear BID PRN for up to 4 days.

***Oral analgesic (see remarks):***

**≥3 yr (able to follow instructions):** Instill several drops of the oral liquid to affected area and expectorate after 2–3 min, **OR** place 10 drops on tongue and mix with saliva, swish for several minutes, and expectorate. Administer up to QID, after meals and QHS, for **up to 7 days**.

**Otic solution: Contraindicated** if tympanic membrane perforated; after otic surgery; ear discharge, drainage, pain, irritation or rash; or PE tubes in place. Tip of applicator should not enter ear canal when used as a cerumenolytic.

**Oral liquid:** Prolonged use may result in fungal overgrowth. **Do not** rinse the mouth or drink for at least 5 min when using oral preparation.

Pregnancy category has not been formally assigned by the FDA.



**CARBINOXAMINE**

Arbinox, Palgic, and generics

**Antihistamine**

No



No



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C

**Liquid:** 4 mg/5 mL (473 mL); may contain propylene glycol**Tabs:** 4 mg**Child (PO [see remarks]):** 0.2–0.4 mg/kg/24 hr PO ÷ TID–QID; alternative dosing by age (**do not exceed** 0.4 mg/kg/24 hr):**2–3 yr:** 2 mg TID–QID**3–6 yr:** 2–4 mg TID–QID**≥6 yr:** 4–6 mg TID–QID**Adult:** 4–8 mg PO TID–QID

Generally not recommended for treating URIs for infants. No proven benefit for infants and young children with URIs. **The FDA does not recommend use for URIs in children <2 yr because of reports of increased fatalities.**



**Contraindicated** in acute asthma, hypersensitivity with other ethanolamine antihistamines, MAO inhibitors, severe hypertension, narrow-angle glaucoma, severe coronary artery disease, and urinary retention. Be aware that combination decongestant products may exist.

May cause drowsiness, vertigo, dry mucus membranes, and headache. Contact dermatitis and CNS excitation have been reported.

**CARNITINE**

Levocarnitine, Carnitor, Carnitor SF, L-Carnitine, and generics

**Nutritional supplement, amino acid**

No



Yes



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B

**Tabs:** 250, 330 mg**Caps:** 250 mg**Oral solution:** 100 mg/mL (118 mL); contains methyl- and propylparabens; Carnitor SF is a sugar-free product.**Injection:** 200 mg/mL (5, 12.5 mL) (preservative free)**Primary carnitine deficiency:****Oral:****Child:** 50–100 mg/kg/24 hr PO ÷ Q8–12 hr; increase slowly as needed and tolerated to **max. dose** of 3 g/24 hr.**Adult:** 330 mg to 1 g/dose BID–TID PO; **max. dose** 3 g/24 hr.**IV:****Child and adult:** 50 mg/kg as loading dose; may follow with 50 mg/kg/24 hr IV infusion (for severe cases); maintenance: 50 mg/kg/24 hr ÷ Q4–6 hr; increase to **max. dose** of 300 mg/kg/24 hr if needed.

May cause nausea, vomiting, abdominal cramps, diarrhea, and body odor. Seizures have been reported in patients with or without a history of seizures. Safety in end-stage renal disease (ESRD) has not been established. High doses to severely compromised renal function or ESRD on dialysis may result in accumulation of potentially toxic metabolites (trimethylamine and trimethylamine-*N*-oxide).



Give bolus IV infusion over 2–3 min.

**CARVEDILOL**

Coreg, Coreg CR, and generics

**Adrenergic antagonist ( $\alpha$  and  $\beta$ ), antihypertensive**

Yes



Yes



?



C

**Tabs:** 3.125, 6.25, 12.5, 25 mg**Extended-release caps (Coreg CR):** 10, 20, 40, 80 mg**Oral suspension:** 0.1, 1.25, 1.67 mg/mL **Heart failure:****Immediate-release dosage forms (tablets and oral suspension (see remarks)):****Infant, child, adolescent:** Start at 0.05–0.2 mg/kg/24 hr PO  $\div$  BID. Dose may be titrated at 1- or 2-wk intervals as needed up to a **maximum** of 2 mg/kg/24 hr or 50 mg/24 hr.

Reported usual effective dose: 0.2–1 mg/kg/24 hr.

**Adult:** Start at 3.125 mg PO BID  $\times$  2 wk; if needed and tolerated, may increase to 6.25 mg BID.Dose may be doubled Q2 wk if needed to the following **maximum doses:****Mild/moderate heart failure:** <85 kg, 25 mg BID;  $\geq$  85 kg, 50 mg BID**Severe heart failure:** 25 mg BID**Extended-release capsules:****Adult:** Start at 10 mg PO once daily  $\times$  2 wk; if needed and tolerated, double the dose Q2 wk up to a **maximum** of 80 mg once daily.**Hypertension:****Adult:****Immediate-release dosage forms:** Start at 6.25 mg PO BID; dose may be doubled every 1–2 wk up to a **maximum** of 25 mg PO BID.**Extended-release capsules:** Start at 20 mg PO once daily  $\times$  1–2 wk; if needed and tolerated, increase to 40 mg PO once daily. If needed, dose may be further increased in 2-wk intervals up to a **maximum** of 80 mg/24 hr.**Contraindicated** in asthma or related bronchospastic disease, sick sinus syndrome, second- or third-degree heart block, severe bradycardia, cardiogenic shock, decompensated cardiac failure requiring IV inotropic therapy, and severe hepatic impairment (Child-Pugh class C).**Use with caution** in mild/moderate hepatic impairment (Child-Pugh class A or B), renal insufficiency, thyrotoxicosis, ischemic heart disease, diabetes, and cataract surgery. **Avoid abrupt withdrawal** of medication.

Children &lt;3.5 years old may have faster carvedilol clearance and may require higher dosages or TID dosing. Carvedilol is a CYP 450 2D6 substrate. Digoxin, disopyramide, and dipyridamole may increase bradycardic effects.

Bradycardia, postural hypotension, peripheral edema, weight gain, hyperglycemia, diarrhea, dizziness, and fatigue are common. Hypersensitivity reactions have been reported. Chest pain, headache, vomiting, edema, and dyspnea have also been reported in children. Administering doses with food can reduce risk for orthostatic hypotension.

**CASPOFUNGIN**

Cancidas

**Antifungal, echinocandin**

Yes



No



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C

**Injection:** 50, 70 mg; contains sucrose (39 mg in 50 mg vial and 54 mg in 70 mg vial)**Preterm neonate—<3 mo infant (based on a small pharmacokinetic study, achieving similar plasma exposure as seen in adults receiving 50 mg/24 hr):** 25 mg/m<sup>2</sup>/dose IV once daily. Alternatively, 1 mg/kg/dose IV once daily  $\times$  2 days, followed by 2 mg/kg/dose IV once daily has been reported in a case series with excellent microbiological results.

CASPOFUNGIN *continued*

**3 mo infant–17 yr (see remarks):** 70 mg/m<sup>2</sup>/dose IV loading dose on day 1, followed by 50 mg/m<sup>2</sup>/dose IV once-daily maintenance dose. Increase maintenance dose to 70 mg/m<sup>2</sup>/dose if response is inadequate or if patient is receiving an enzyme-inducing medication (see remarks).

**Maximum loading and maintenance dose:** 70 mg/dose

**Adolescent and adult (see remarks):**

**Loading dose:** 70 mg IV  $\times$  1

**Maintenance dose:**

**Usual:** 50 mg IV once daily. If tolerated and response is inadequate or if patient is receiving an enzyme-inducing medication (see remarks), increase to 70 mg IV once daily.

**Hepatic insufficiency (Child-Pugh score 7–9):** 35 mg IV once daily

**Use with caution** in hepatic impairment and concomitant enzyme-inducing drugs. Higher maintenance doses (70 mg/m<sup>2</sup>/dose in children and 70 mg in adults) are recommended for concomitant use of enzyme inducers, such as carbamazepine, dexamethasone, phenytoin, nevirapine, efavirenz, or rifampin. Use Mosteller formula for calculating BSA.

Most common adverse effects (>10%) in children include fever, diarrhea, rash, elevated ALT/AST, hypokalemia, hypotension, and chills. May also cause facial swelling, nausea/vomiting, headache, infusion site phlebitis, and LFT elevation. Anaphylaxis and possible histamine-related reactions (angioedema, bronchospasm, and warmth sensation) have been reported. Hepatobiliary adverse effects have been reported in pediatric patients with serious underlying medical conditions.

Reduce daily dose by 30% in moderate hepatic impairment (Child-Pugh score 7–9).

Use with cyclosporine may cause transient increase in LFTs and caspofungin level elevations. May decrease tacrolimus levels.

Administer doses by slow IV infusion over 1 hr. **Do not** mix or co-infuse with other medications, and **avoid** using dextrose-containing diluents (e.g., D<sub>5</sub>W).

**CEFACLOR**

Ceclor, Ceclor CD, Raniclor, and generics

**Antibiotic, cephalosporin (second generation)**



No



Yes



1



B

**Caps:** 250, 500 mg

**Extended-release tabs (Ceclor CD):** 500 mg

**Chewable tabs (Raniclor):** 125, 187, 250, 375 mg; contains phenylalanine

**Oral suspension:** 125 mg/5 mL (75, 150 mL), 187 mg/5 mL (100 mL), 250 mg/5 mL (75, 150 mL), 375 mg/5 mL (100 mL)

**Child > 1 mo old (use regular-release dosage forms):** 20–40 mg/kg/24 hr PO  $\div$  Q8 hr; **max. dose** 2 g/24 hr

**Q12 hr dosage interval option for otitis media:** 40 mg/kg/24 hr

**Q12 hr dosage interval option for pharyngitis:** 20 mg/kg/24 hr

**Adult:** 250–500 mg/dose PO Q8 hr; **max. dose** 4 g/24 hr

**Extended-release tablets:** 500 mg/dose PO Q12 hr



**Use with caution** in patients with penicillin allergy or renal impairment. Side effects include elevated LFTs, bone marrow suppression, and moniliasis. Probenecid may increase cefaclor concentrations. May cause positive Coombs test or false-positive test for urinary glucose.

Serum sickness reactions have been reported in patients receiving multiple courses of cefaclor.

**Do not** crush, cut, or chew extended-release tablets. Doses should be given on an empty stomach.

**Extended-release tablets not recommended for children. Adjust dose in renal failure (see Chapter 31).**



**CEFADROXIL**

Duricef and generics

**Antibiotic, cephalosporin (first generation)**

No



Yes



1



B

**Oral suspension:** 250, 500 mg/5 mL (75, 100 mL)**Tabs:** 1 g**Caps:** 500 mg**Infant and child:** 30 mg/kg/24 hr PO ÷ Q12 hr (daily dose may be administered once daily for group A  $\beta$ -hemolytic streptococci pharyngitis/tonsillitis); **max. dose** 2 g/24 hr**Bacterial endocarditis prophylaxis for dental and upper airway procedures:** 50 mg/kg/dose (max. dose 2 g)  $\times$  1 PO 1 hr before procedure**Adolescent and adult:** 1–2 g/24 hr PO ÷ Q12–24 hr (administer Q12 hr for complicated UTIs); **max. dose** 2 g/24 hr**Bacterial endocarditis prophylaxis for dental and upper airway procedures:** 2 g  $\times$  1 PO 1 hr before procedureSee *Cephalexin* for **precautions** and interactions. Rash, nausea, vomiting, and diarrhea are common. Transient neutropenia, and vaginitis have been reported. **Adjust dose in renal failure** (see Chapter 31).**CEFAZOLIN**

Ancef, Zolicef, and generics

**Antibiotic, cephalosporin (first generation)**

Yes



Yes



1



B

**Injection:** 0.5, 1, 5, 10, 20 g**Frozen injection:** 1 g/50 mL 5% dextrose (iso-osmotic solution)

Contains 2.1 mEq Na/g drug

**Neonate IM, IV:****Postnatal age  $\leq$  7 days:** 40 mg/kg/24 hr ÷ Q12 hr**Postnatal age  $>$  7 days:** **$\leq$ 2000 g:** 40 mg/kg/24 hr ÷ Q12 hr **$>$ 2000 g:** 60 mg/kg/24 hr ÷ Q8 hr**Infant  $>$  1 mo and child:** 50–100 mg/kg/24 hr ÷ Q6–8 hr IV/IM; **max. dose** 6 g/24 hr**Adult:** 2–6 g/24 hr ÷ Q6–8 hr IV/IM; **max. dose** 12 g/24 hr**Bacterial endocarditis prophylaxis for dental and upper respiratory procedures:****Infant and child:** 50 mg/kg IV/IM (max. dose 1 g) 30 min before procedure**Adult:** 1 g IV/IM 30 min before procedure**Use with caution** in renal impairment or in penicillin-allergic patients. Does not penetrate well into CSF. May cause phlebitis, leukopenia, thrombocytopenia, transient liver enzyme elevation, and false-positive urine reducing substance (Clinitest) and Coombs tests.For dosing in obese patients, use higher end of the dosing recommendation. **Adjust dose in renal failure** (see Chapter 31).

**CEFDINIR**

Omnicef

**Antibiotic, cephalosporin (third generation)**

No



Yes



1



B

**Caps:** 300 mg**Oral suspension:** 125 mg/5 mL (60, 100 mL), 250 mg/5 mL (60, 100 mL)**6 mo–12 yr:****Otitis media, sinusitis, pharyngitis/tonsillitis:** 14 mg/kg/24 hr PO ÷ Q12–24 hr;**max. dose** 600 mg/24 hr**Uncomplicated skin infections (see remarks):** 14 mg/kg/24 hr PO ÷ Q12 hr; **max. dose** 600 mg/24 hr**≥13 yr and adult:****Bronchitis, sinusitis, pharyngitis/tonsillitis:** 600 mg/24 hr PO ÷ Q12–24 hr**Community-acquired pneumonia, uncomplicated skin infections (see remarks):** 600 mg/24 hr PO ÷ Q12 hr

**Use with caution** in penicillin-allergic patients or in presence of renal impairment. Good gram-positive cocci activity. May cause diarrhea (especially in children <2 yr), headache, vaginitis, and false-positive urine reducing substance (Clinitest) and Coombs tests. Eosinophilia and abnormal liver function tests have been reported with higher than usual doses.

Once-daily dosing has not been evaluated in pneumonia and skin infections. Probenecid increases serum cefdinir levels. Avoid concomitant administration with iron and iron-containing vitamins and antacids containing aluminum or magnesium (space by 2 hr apart) to reduce risk for decreasing antibiotic's absorption. Doses may be taken without regard to food. **Adjust dose in renal failure (see Chapter 31).**

**CEFEPIME**

Maxipime and generics

**Antibiotic, cephalosporin (fourth generation)**

No



Yes



1



B

**Injection:** 0.5, 1, 2 g**Premixed injection:** 1 g/50 mL, 2 g/100 mL (iso-osmotic dextrose solution)

Each 1 g drug contains 725 mg L-arginine.

**Neonate:****<14 days:** 60 mg/kg/24 hr ÷ Q12 hr IV/IM**≥14 days:** 100 mg/kg/24 hr ÷ Q12 hr IV/IM. For meningitis or *Pseudomonas* infections, use 150 mg/kg/24 hr ÷ Q8 hr IV/IM**Child ≥ 2 mo:** 100 mg/kg/24 hr ÷ Q12 hr IV/IM**Meningitis, fever, and neutropenia, or serious infections:** 150 mg/kg/24 hr ÷ Q8 hr IV/IM.**Max. dose:** 6 g/24 hr**Cystic fibrosis:** 150 mg/kg/24 hr ÷ Q8 hr IV/IM, up to a **max. dose** of 6 g/24 hr**Adult:** 1–4 g/24 hr ÷ Q12 hr IV/IM**Severe infections:** 6 g/24 hr ÷ Q8 hr IV/IM**Max. dose:** 6 g/24 hr

**Use with caution** in patients with penicillin allergy or renal impairment. Good activity against *Pseudomonas aeruginosa* and other gram-negative bacteria, plus most gram-positives (methicillin-sensitive *Staphylococcus aureus* [MRSA]). May cause thrombophlebitis, gastrointestinal discomfort, transient increases in liver enzymes, and false-positive urine reducing substance (Clinitest) and Coombs tests. Probenecid increases serum cefepime levels. Encephalopathy, myoclonus, seizures (including nonconvulsive status epilepticus), transient leukopenia, neutropenia, agranulocytosis, and thrombocytopenia have been reported. **Adjust dose in renal failure (see Chapter 31).**



**CEFIXIME**

Suprax

**Antibiotic, cephalosporin (third generation)**

No



Yes



1



B

**Oral suspension:** 100 mg/5 mL (50, 75 mL)**Tab:** 400 mg**Infant (>6 mo) and child:** 8 mg/kg/24 hr ÷ Q12–24 hr PO; **max. dose** 400 mg/24 hr**Acute UTI:** 16 mg/kg/24 hr ÷ Q12 hr on day 1, followed by 8 mg/kg/24 hr Q24 hr PO × 13 days. **Max. dose** 400 mg/24 hr**Sexual victimization prophylaxis:** 8 mg/kg PO × 1 (**max. dose** 400 mg) PLUS azithromycin 20 mg/kg PO × 1 (**max. dose** 1 g)**Adolescent and adult:** 400 mg/24 hr ÷ Q12–24 hr PO**Uncomplicated cervical, urethral, or rectal infections due to *Neisseria gonorrhoeae*:** 400 mg × 1 PO PLUS azithromycin 1 g PO × 1 **OR** doxycycline 100 mg PO BID × 7 days**Sexual victimization prophylaxis:** 400 mg PO × 1 PLUS azithromycin 1 g PO × 1 **OR** doxycycline 100 mg BID PO × 7 days, PLUS metronidazole 2 g PO × 1, PLUS hepatitis B vaccine (if not immunized)

**Use with caution** in patients with penicillin allergy or renal failure. Adverse reactions include diarrhea, abdominal pain, nausea, and headaches. Because of reduced bioavailability, **do not** use tablets for treatment of otitis media. Probenecid increases serum cefixime levels. Unlike most cephalosporins, drug is excreted unchanged in bile (5%–10%) and urine (50%). May increase carbamazepine serum concentrations. May cause false-positive urine reducing substance test (Clinitest), Coombs test, and nitroprusside test for ketones. **Adjust dose in renal failure (see Chapter 31).**

**CEFOTAXIME**

Claforan and generics

**Antibiotic, cephalosporin (third generation)**

No



Yes



1



B

**Injection:** 0.5, 1, 2, 10 g**Frozen injection:** 1 g/50 mL 3.4% dextrose, 2 g/50 mL 1.4% dextrose (iso-osmotic solutions)

Contains 2.2 mEq Na/g drug

**Neonate: IV/IM:****Postnatal age ≤ 7 days:**

&lt;2000 g: 100 mg/kg/24 hr ÷ Q12 hr

≥2000 g: 100–150 mg/kg/24 hr ÷ Q8–12 hr

**Postnatal age > 7 days:**

&lt;1200 g: 100 mg/kg/24 hr ÷ Q12 hr

1200–2000 g: 150 mg/kg/24 hr ÷ Q8 hr

&gt;2000 g: 150–200 mg/kg/24 hr ÷ Q6–8 hr

**Infant and child (1 mo–12 yr and <50 kg):** 100–200 mg/kg/24 hr ÷ Q6–8 hr IV/IM. Higher doses of 150–225 mg/kg/24 hr ÷ Q6–8 hr have been recommended for infections outside CSF due to penicillin-resistant pneumococci.

**Meningitis:** 200 mg/kg/24 hr ÷ Q6 hr IV/IM. Higher doses of 225–300 mg/kg/24 hr ÷ Q6–8 hr, in combination with vancomycin (dosed at CNS target levels), have been recommended for meningitis due to penicillin-resistant pneumococci.

**Max. dose:** 12 g/24 hr**Child (>12 yr or ≥50 kg) and adult:** 1–2 g/dose Q6–8 hr IV/IM**Severe infection:** 2 g/dose Q4–6 hr IV/IM**Max. dose:** 12 g/24 hr**Uncomplicated gonorrhea:** 0.5–1 g × 1 IM

CEFOTAXIME *continued*

**Use with caution** in penicillin allergy and renal impairment (reduce dosage). Toxicities similar to other cephalosporins: allergy, neutropenia, thrombocytopenia, eosinophilia, false-positive urine reducing substance (Clinitest) and Coombs tests, and elevated BUN, creatinine, and liver enzymes. Probenecid increases serum cefotaxime levels.

Good CNS penetration. **Adjust dose in renal failure (see Chapter 31).**

**CEFOTETAN**

Cefotan and generics

**Antibiotic, cephalosporin (second generation)**



No



Yes



1



B

**Injection:** 1, 2, 10 g

**Frozen injection:** 1 g/50 mL 3.8% dextrose, 2 g/50 mL 2.2% dextrose (iso-osmotic solutions)

Contains 3.5 mEq Na/g drug

**Infant and child (limited data):** 40–80 mg/kg/24 hr ÷ Q12 hr IV/IM

**Adolescent and adult:** 2–4 g/24 hr ÷ Q12 hr IV/IM

**PID:** 2 g Q12 hr IV × 24–48 hr after clinical improvement with doxycycline 100 mg Q12 hr PO/IV × 14 days

**Max. dose (all ages):** 6 g/24 hr

**Preoperative prophylaxis (30–60 min before procedure):**

**Child:** 40 mg/kg/dose (max. dose 2 g/dose) IV

**Adult:** 1–2 g IV

**Use with caution** in penicillin-allergic patients or in presence of renal impairment. Has good anaerobic activity. May cause disulfiram-like reaction with ethanol, increase effects/toxicities of anticoagulants, false-positive urine reducing substance test (Clinitest), and false elevations of serum and urine creatinine (Jaffe method). Hemolytic anemia has been reported. Good anaerobic activity but poor CSF penetration. **Adjust dose in renal failure (see Chapter 31).**

**CEFOXITIN**

Mefoxin and generics

**Antibiotic, cephalosporin (second generation)**



No



Yes



1



B

**Injection:** 1, 2, 10 g

**Frozen injection:** 1 g/50 mL 4% dextrose, 2 g/50 mL 2.2% dextrose (iso-osmotic solutions)

Contains 2.3 mEq Na/g drug

**Neonate:** 90–100 mg/kg/24 hr ÷ Q8 hr IM/IV

**Infant and child:**

**Mild/moderate infections:** 80–100 mg/kg/24 hr ÷ Q6–8 hr IM/IV

**Severe infections:** 100–160 mg/kg/24 hr ÷ Q4–6 hr IM/IV

**Adult:** 1–2 g/dose Q6–8 hr IM/IV

**PID:** 2 g IV Q6h × 24–48 hr after clinical improvement. Doxycycline 100 mg Q12 hr PO/IV × 14 days is also initiated at the same time.

**Max. dose (all ages):** 12 g/24 hr

**Use with caution** in penicillin-allergic patients or in presence of renal impairment. Has good anaerobic activity but poor CSF penetration. Probenecid increases serum cefoxitin levels. May cause false-positive urine reducing substance tests (Clinitest and other copper reduction methods) and false elevations of serum and urine creatinine (Jaffe and KDA methods).

**Adjust dose in renal failure (see Chapter 31).**

**CEFPODOXIME PROXETIL**

Vantin and generics

**Antibiotic, cephalosporin (third generation)**

No



Yes



1



B

**Tab:** 100, 200 mg**Oral suspension:** 50, 100 mg/5 mL (50, 75, 100 mL)**2 mo–12 yr:****Otitis media:** 10 mg/kg/24 hr PO ÷ Q12–24 hr × 5 days; **max. dose** 400 mg/24 hr**Pharyngitis/tonsillitis:** 10 mg/kg/24 hr PO ÷ Q12 hr × 5–10 days; **max. dose** 200 mg/24 hr**Acute maxillary sinusitis:** 10 mg/kg/24 hr PO ÷ Q12 hr × 10 days; **max. dose** 400 mg/24 hr**≥13 yr–adult:****Exacerbation of chronic bronchitis, community-acquired pneumonia, and sinusitis:** 400 mg/24 hr PO ÷ Q12 hr × 10 days (14 days for pneumonia)**Pharyngitis/tonsillitis:** 200 mg/24 hr PO ÷ Q12 hr × 5–10 days**Skin/skin structure infection:** 800 mg/24 hr PO ÷ Q12 hr × 7–14 days**Uncomplicated gonorrhea:** 200 mg PO × 1**Use with caution** in penicillin-allergic patients or in presence of renal impairment. May cause diarrhea, nausea, vomiting, vaginal candidiasis, and false-positive Coombs test.Tablets should be administered with food to enhance absorption. Suspension may be administered without regard to food. High doses of antacids or H<sub>2</sub> blockers may reduce absorption. Probenecid increases serum cefpodoxime levels.**Adjust dose in renal failure (see Chapter 31).****CEFPROZIL**

Cefzil and generics

**Antibiotic, cephalosporin (second generation)**

No



Yes



1



B

**Tab:** 250, 500 mg**Oral suspension:** 125 mg/5 mL, 250 mg/5 mL (50, 75, 100 mL); contains aspartame and phenylalanine**Otitis media:****6 mo–12 yr:** 30 mg/kg/24 hr PO ÷ Q12 hr**Pharyngitis/tonsillitis:****2–12 yr:** 15 mg/kg/24 hr PO ÷ Q12 hr**Acute sinusitis:****6 mo–12 yr:** 15–30 mg/kg/24 hr PO ÷ Q12–24 hr**Uncomplicated skin infections:****2–12 yr:** 20 mg/kg/24 hr PO Q24 hr**Other:****≥13 yr and adult:** 500–1000 mg/24 hr PO ÷ Q12–24 hr**Max. dose** (all ages): 1 g/24 hr**Use with caution** in penicillin-allergic patients or in presence of renal impairment. Oral suspension contains aspartame and phenylalanine and should not be used by phenylketonurics. May cause nausea, vomiting, diarrhea, liver enzyme elevations, and false-positive urine reducing substance tests (Clinitest and other copper reduction methods) and Coombs test. Probenecid increases serum cefprozil levels. Absorption not affected by food.  
**Adjust dose in renal failure (see Chapter 31).**

**CEFTAZIDIME**

Fortaz, Tazidime, Tazicef, Ceptaz (arginine salt), and generics

**Antibiotic, cephalosporin (third generation)**



No



Yes



1



B

**Injection:** 0.5, 1, 2, 6, 10 g

**Frozen injection:** 1 g/50 mL 4.4% dextrose, 2 g/50 mL 3.2% dextrose (iso-osmotic solutions)

(Fortaz, Tazicef, Tazidime contains 2.3 mEq Na/g drug)

(Ceptaz contains 349 mg L-arginine/g drug)

**Neonate (IV/IM):**

**Postnatal age  $\leq 7$  days:**

**<2000 g:** 100 mg/kg/24 hr  $\div$  Q12 hr

**$\geq 2000$  g:** 100–150 mg/kg/24 hr  $\div$  Q8–12 hr

**Postnatal age  $> 7$  days:**

**<1200 g:** 100 mg/kg/24 hr  $\div$  Q12 hr

**$\geq 1200$  g:** 150 mg/kg/24 hr  $\div$  Q8 hr

**Infant ( $> 1$  mo) and child:** 100–150 mg/kg/24 hr  $\div$  Q8 hr IV/IM; **max. dose** 6 g/24 hr

**Cystic fibrosis and meningitis:** 150 mg/kg/24 hr  $\div$  Q8 hr IV/IM; **max. dose** 6 g/24 hr

**Adult:** 1–2 g/dose Q8–12 hr IV/IM; **max. dose** 6 g/24 hr

**Use with caution** in penicillin-allergic patients or in presence of renal impairment. Good

*Pseudomonas* coverage and CSF penetration. May cause rash, liver enzyme elevations, and false-positive urine reducing substance tests (Clinitest and other copper reduction methods) and Coombs test. Probenecid increases serum ceftazidime levels. **Adjust dose in renal failure (see Chapter 31).**

**CEFTIBUTEN**

Cedax

**Antibiotic, cephalosporin (third generation)**



No



Yes



1



B

**Oral suspension:** 90 mg/5 mL (60, 90, 120 mL), 180 mg/5 mL (60 mL); contains sodium benzoate

**Caps:** 400 mg

**Child ( $> 6$  mo):**

**Otitis media and pharyngitis/tonsillitis:** 9 mg/kg/24 hr (**max. dose** 400 mg/24 hr) PO once daily  $\times$  10 days

**$\geq 12$  yr and adult:** 400 mg PO once daily  $\times$  10 days; **max. dose** 400 mg/24 hr

**Use with caution** in penicillin-allergic patients or in presence of renal impairment. May cause GI symptoms and elevations in eosinophils and BUN. Stevens-Johnson syndrome has been reported. Gastric acid-lowering medications (e.g., ranitidine, omeprazole) may enhance bioavailability of ceftibuten.

Oral suspension should be administered 2 hr before or 1 hr after a meal. **Adjust dose in renal failure (see Chapter 31).**

**CEFTRIAXONE**

Rocephin and generics

**Antibiotic, cephalosporin (third generation)**

Yes



Yes



1



B

**Injection:** 0.25, 0.5, 1, 2, 10 g**Frozen injection:** 1 g/50 mL 3.8% dextrose, 2 g/50 mL 2.4% dextrose (iso-osmotic solutions)

Contains 3.6 mEq Na/g drug

**Neonate:*****Gonococcal ophthalmia or prophylaxis:*** 25–50 mg/kg/dose IM/IV  $\times$  1; **max. dose** 125 mg/dose**Infant (>1 mo) and child:*****Mild/moderate infections:*** 50–75 mg/kg/24 hr  $\div$  Q12–24 hr IM/IV; **max. dose** 2 g/24 hr***Meningitis (including penicillin-resistant pneumococci):*** 100 mg/kg/24 hr IM/IV  $\div$  Q12 hr; **max. dose** 2 g/dose and 4 g/24 hr***Penicillin-resistant pneumococci outside of CSF:*** 80–100 mg/kg/24 hr  $\div$  Q12–24 hr; **max. dose** 2 g/dose and 4 g/24 hr***Acute otitis media:*** 50 mg/kg IM  $\times$  1; **max. dose** 1 g***Adult:*** 1–2 g/dose Q12–24 hr IV/IM; **max. dose** 2 g/dose and 4 g/24 hr***Uncomplicated gonorrhea or chancroid:*** 250 mg IM  $\times$  1**Bacterial endocarditis prophylaxis for dental and upper respiratory procedures:*****Infant and child:*** 50 mg/kg IV/IM (**max. dose** 1 g) 30 min before procedure***Adult:*** 1 g IV/IM 30 min before procedure

**Contraindicated** in neonates with hyperbilirubinemia. **Do not** administer with IV calcium-containing solutions or products (mixed or administered simultaneously via different lines) in neonates (<28 days old) because of risk of precipitation of ceftriaxone-calcium salt. Cases of fatal reactions with calcium-ceftriaxone precipitates in lung and kidneys in term and preterm neonates have been reported. **Do not** administer simultaneously with IV calcium-containing solutions via a Y-site for any age group. IV calcium-containing products may be administered sequentially only when the infusion lines are thoroughly flushed between infusions with a compatible fluid.

**Use with caution** in penicillin allergy; patients with gallbladder, biliary tract, liver, or pancreatic disease; presence of renal impairment; or in neonates with continuous dosing (risk for hyperbilirubinemia). In neonates, consider using an alternative third-generation cephalosporin with similar activity. Unlike other cephalosporins, ceftriaxone is significantly cleared by the biliary route (35%–45%).

Rash, injection site pain, diarrhea, and transient increase in liver enzymes are common. May cause reversible cholelithiasis, sludging in gallbladder, and jaundice. May interfere with serum and urine creatinine assays (Jaffe method) and cause false-positive urinary protein and urinary reducing substances (Clinitest).

For IM injections, dilute drug with either sterile water for injection or 1% lidocaine to a concentration of 250 or 350 mg/mL (250 mg/mL has lower incidence of injection site reactions). Assess potential risk/benefit for using lidocaine as a diluent; see *Lidocaine* for additional remarks.

**CEFUROXIME (IV, IM)/CEFUROXIME AXETIL (PO)**  
**CEFUROXIME AXETIL (PO)**

IV: Zinacef and generics

PO: Ceftin and generics

*Antibiotic, cephalosporin (second generation)*

No



Yes



1



B

**Injection:** 0.75, 1.5, 7.5 g**Frozen injection:** 1.5 g/50 mL water (iso-osmotic solutions)

Injectable dosage forms contain 2.4 mEq Na/g drug

**Tabs:** 250, 500 mg**Oral suspension:** 125, 250 mg/5 mL (50, 100 mL); may contain aspartame**IM/IV:****Neonate:** 50–100 mg/kg/24 hr ÷ Q12 hr**Infant (>3 mo)/child:** 75–150 mg/kg/24 hr ÷ Q8 hr**Adult:** 750–1500 mg/dose Q8 hr**Max. dose:** 9 g/24 hr**PO (see remarks):****Child (3 mo–12 yr):****Pharyngitis and tonsillitis:****Oral suspension:** 20 mg/kg/24 hr ÷ Q12 hr; **max. dose** 500 mg/24 hr**Tabs:** 125 mg PO Q12 hr**Otitis media, impetigo, and maxillary sinusitis:****Oral suspension:** 30 mg/kg/24 hr ÷ Q12 hr; **max. dose** 1 g/24 hr**Tabs:** 250 mg Q12 hr**Lyme disease (alternative to doxycycline or amoxicillin):****Oral suspension:** 30 mg/kg/24 hr (**max. dose** 500 mg/24 hr) ÷ Q12 hr × 14–28 days**Child (≥13 yr):****Sinusitis, otitis media, pharyngitis, and tonsillitis:****Tabs:** 250 mg Q12 hr**Adult:** 250–500 mg BID; **max. dose** 1 g/24 hr

**Use with caution** in penicillin-allergic patients or in presence of renal impairment. May cause GI discomfort; thrombophlebitis at infusion site; false-positive urine reducing substance tests (Clinitest and other copper reduction methods) and Coombs test; and may interfere with serum and urine creatinine determinations by the alkaline picrate method. **Not recommended for meningitis.**

Tablets and oral suspension are **NOT** bioequivalent and are **NOT** substitutable on a mg/mg basis.

Administer suspension with food. Concurrent use of antacids, H<sub>2</sub> blockers, and proton-pump inhibitors may decrease oral absorption. **Adjust dose in renal failure (see Chapter 31).**

**CEPHALEXIN**

Keflex and generics

**Antibiotic, cephalosporin (first generation)**

No



Yes



1



B

**Caps:** 250, 500, 750 mg**Tabts:** 250, 500 mg**Oral suspension:** 125 mg/5 mL, 250 mg/5 mL (100, 200 mL)**Infant and child:** 25–100 mg/kg/24 hr PO ÷ Q6 hr. Less frequent dosing (Q8–12 hr) can be used for uncomplicated infections.**Otitis media:** 75–100 mg/kg/24 hr PO ÷ Q6 hr.**Streptococcal pharyngitis and skin infections:** 25–50 mg/kg/24 hr PO ÷ Q6–12 hr. Total daily dose may be divided Q12 hr for streptococcal pharyngitis (>1 yr).**Adult:** 1–4 g/24 hr PO ÷ Q6 hr**Max. dose (all ages):** 4 g/24 hr**Bacterial endocarditis prophylaxis for dental and upper respiratory procedures:****Infant and child:** 50 mg/kg PO (**max. dose** 2 g) 1 hr before procedure**Adult:** 2 g PO 1 hr before procedure

Some cross-reactivity with penicillins. **Use with caution** in renal insufficiency. May cause GI discomfort, false-positive urine reducing substance tests (Clinitest and other copper reduction methods) and Coombs test, false elevation of serum theophylline levels (HPLC method), and false urinary protein test. Probenecid increases serum cephalexin levels, and concomitant administration with cholestyramine may reduce cephalexin absorption. May increase effects of metformin.

Administer doses on an empty stomach, 2 hr before or 1 hr after meals. **Adjust dose in renal failure** (see Chapter 31).

**CETIRIZINE ± PSEUDOEPHEDRINE**

Zyrtec, Children's Zyrtec, and generics

In combination with pseudoephedrine: Zyrtec-D 12 Hour

**Antihistamine, less sedating**

Yes



Yes



?



B/C

**Oral solution or syrup [OTC]:** 5 mg/5 mL (120, 473 mL)**Tabts [OTC]:** 5, 10 mg**Capsule (Liquid-filled [OTC]):** 10 mg**Chewable tabs [OTC]:** 5, 10 mg**In combination with pseudoephedrine (PE):****Extended-release tabs** (Zyrtec-D 12 Hour [OTC]): 5 mg cetirizine + 120 mg PE**Cetirizine (see remarks for dosing in hepatic impairment):****6 mo and <2 yr:** 2.5 mg PO once daily; dose may be increased for children 12–23 mo to a **max. dose** of 2.5 mg PO Q12 hr.**2–5 yr:** Initial dose, 2.5 mg PO once daily; if needed, may increase dose to a **max. dose** of 5 mg/24 hr once daily or divided BID.**≥6 yr–adult:** 5–10 mg PO once daily.**Cetirizine in combination with pseudoephedrine (PE) (see remarks for dosing in hepatic impairment):****≥12 yr and adult:** Zyrtec-D 12 Hour: 1 tablet PO BID

CETIRIZINE ± PSEUDOEPHEDRINE *continued*

Generally **not recommended** for treating URIs for infants. No proven benefit for infants and young children with URIs. **The FDA does not recommend use for URIs in children <2 yr because of reports of increased fatalities.**

May cause headache, pharyngitis, GI symptoms, dry mouth, and sedation. Aggressive reactions and convulsions have been reported. Has **NOT** been implicated in causing cardiac arrhythmias when used with other drugs that are metabolized by hepatic microsomal enzymes (e.g., ketoconazole, erythromycin).

**In hepatic impairment, the following doses have been recommended:**

**Cetirizine:**

**<6 yr:** Use **not recommended**

**6–11 yr:** <2.5 mg PO once daily

**≥12 yr–adult:** 5 mg PO once daily

**Cetirizine in combination with pseudoephedrine:**

**≥12 yr–adult:** 1 tablet PO once daily

Doses may be administered without regard to food. For Zyrtec-D 12 Hour, see *Pseudoephedrine* for additional remarks. Pregnancy category is “B” for cetirizine and “C” when combined with pseudoephedrine. **Dosage adjustment is recommended in renal impairment (see Chapter 31).**

**CHARCOAL, ACTIVATED**

See Chapter 2

**CHLORAL HYDRATE**

Aquachloral Suppettes and generics

**Sedative, hypnotic**



Yes



Yes



2



C

**Oral suspension:** 100 mg/mL

Check with your pharmacy for availability of this medication in the United States.

**Infant and child:**

**Sedative:** 25–50 mg/kg/24 hr PO/PR ÷ Q6–8 hr; **max. dose** 500 mg/dose

**Sedation for procedures:** 50–75 mg/kg/dose PO/PR 30–60 min before procedure; may repeat in 30 min if needed to up to a total **max. dose** of 120 mg/kg or 1 g total for infants and 2 g total for children

**Adult:**

**Sedative:** 250 mg/dose TID PO/PR

**Hypnotic:** 500–1000 mg/dose PO/PR; **max. dose** 2 g/24 hr



**Contraindicated** in patients with hepatic or renal disease. **Avoid** use if GFR < 50 mL/min (see Chapter 31). **Use with caution** in combination with IV furosemide (vasodilation) or warfarin (potentiates warfarin). May cause GI irritation, paradoxical excitement, hypotension, and myocardial/respiratory depression. Chronic administration in neonates can lead to accumulation of active metabolites. Requires same monitoring as other sedatives.

Has no analgesic effects. Peak effects occur within 30–60 min. **Do not exceed** 2 wk of chronic use.

**Avoid** use in moderate/severe renal failure. Sudden withdrawal may cause delirium tremens.





**CHLORAMPHENICOL**

Chloromycetin and generics

**Antibiotic**

Yes



Yes



3



C

**Injection:** 1 g

Contains 2.25 mEq Na/g drug

**Neonate IV:****Loading dose:** 20 mg/kg**Maintenance dose (first dose should be given 12 hours after loading dose):**

≤7 days: 25 mg/kg/24 hr Q24 hr

&gt;7 days:

≤2 kg: 25 mg/kg/24 hr Q24 hr

&gt;2 kg: 50 mg/kg/24 hr ÷ Q12 hr

**Infant/child/adult:** 50–75 mg/kg/24 hr IV ÷ Q6 hr**Meningitis:** 75–100 mg/kg/24 hr IV ÷ Q6 hr**Max. dose** (all ages): 4 g/24 hr

Dose recommendations are merely guidelines for therapy; monitoring of blood levels is essential. Follow hematologic status for dose-related or idiosyncratic marrow suppression. “Gray baby” syndrome may be seen with levels >50 mg/L. **Use with caution** in G6PD deficiency, renal or hepatic dysfunction, and neonates.

Concomitant use of phenobarbital and rifampin may lower chloramphenicol serum levels. Phenytoin may increase chloramphenicol serum levels. Chloramphenicol may increase effects/toxicity of phenytoin, chlorpropamide, cyclosporine, tacrolimus, and oral anticoagulants; may decrease absorption of vitamin B<sub>12</sub>. Chloramphenicol is an inhibitor of CYP 450 2C9.

Therapeutic levels: Peak, 15–25 mg/L for meningitis; 10–20 mg/L for other infections. Trough, 5–15 mg/L for meningitis; 5–10 mg/L for other infections. Recommended serum sampling time: trough (IV/PO), within 30 min before next dose; peak (IV), 30 min after the end of infusion. Time to achieve steady state: 2–3 days for newborns, 12–24 hr for children and adults. **NOTE:** Higher serum levels may be achieved using oral rather than IV route.

**CHLOROQUINE PHOSPHATE**

Aralen and generics

**Amebicide, antimalarial**

Yes



Yes



2



C

**Tabs:** 250, 500 mg as phosphate (150, 300 mg base, respectively)**Oral suspension:** 16.67 mg/mL as phosphate (10 mg/mL base), 15 mg/mL as phosphate (9 mg/mL base) **Doses expressed in mg of chloroquine base:****Malaria prophylaxis (start 1 wk before exposure and continue for 4 wk after leaving endemic area):****Infant and child:** 5 mg/kg/dose PO every wk; **max. dose** 300 mg/dose**Adult:** 300 mg/dose PO every wk**Malaria treatment (chloroquine-sensitive strains):**For treatment for malaria, consult with ID specialist or see latest edition of AAP *Red Book*.**Infant and child:** 10 mg/kg/dose (**max. dose** 600 mg/dose) PO × 1, followed by 5 mg/kg/dose (**max. dose** 300 mg/dose) 6 hr later, and then once daily for 2 days.**Adult:** 600 mg/dose PO × 1, followed by 300 mg/dose 6 hr later, and then once daily for 2 days.

CHLOROQUINE PHOSPHATE *continued*

**Use with caution** in liver disease, preexisting auditory damage or seizures, G6PD deficiency, psoriasis, porphyria, or concomitant hepatotoxic drugs. May cause nausea, vomiting, ECG abnormalities, prolonged QT interval, blurred vision, retinal and corneal changes (reversible corneal opacities), headaches, confusion, skeletal muscle weakness, increased liver enzymes, and hair depigmentation. Steven-Johnson syndrome, TEN, and anaphylactic reactions have been reported.

Antacids, ampicillin, and kaolin may decrease absorption of chloroquine (allow 4-hr interval between these drugs and chloroquine). Cimetidine may increase effects/toxicity of chloroquine. May increase serum cyclosporine levels. Coadministration with mefloquine may increase risk of convulsions. May reduce antibody response to intradermal human diploid-cell rabies vaccine.

**Adjust dose in renal failure (see Chapter 31).**

**CHLOROTHIAZIDE**

Diuril and generics

**Thiazide diuretic**



Yes



Yes



2



C/D

**Tabs:** 250, 500 mg

**Oral suspension:** 250 mg/5 mL (237 mL); contains 0.5% alcohol, 0.12% methylparaben, 0.02% propylparaben, and 0.1% benzoic acid

**Injection:** 500 mg; contains 5 mEq Na/1 g drug

**<6 mo:**

**PO:** 20–40 mg/kg/24 hr ÷ Q12 hr

**IV:** Start at 2–8 mg/kg/24 hr ÷ Q12 hr, may increase to 20–40 mg/kg/24 hr ÷ Q12 hr if needed.

**≥6 mo:**

**PO:** 10–20 mg/kg/24 hr ÷ Q12 hr; **maximum PO dose** by age:

**6 mo–2 yr:** 375 mg/24 hr

**2–12 yr:** 1 g/24 hr

**>12 yr:** 2 g/24 hr

**IV:** Start at 4 mg/kg/24 hr ÷ Q12–24 hr; may increase to 20 mg/kg/24 hr ÷ Q12 hr if needed.

**Adult:** 500–2000 mg/24 hr ÷ Q12–24 hr PO/IV; alternative IV dosing: some may respond to intermittent dosing on alternate days or on 3–5 days each wk.

**Use with caution** in liver and severe renal disease. May increase serum calcium, bilirubin, glucose, and uric acid. May cause alkalosis, pancreatitis, dizziness, hypokalemia, and hypomagnesemia.

**Avoid IM or SC administration.**

Pregnancy category changes to D if used in pregnancy-induced hypertension.

**CHLORPHENIRAMINE MALEATE/DEXCHLORPHENIRAMINE MALEATE**

Chlorpheniramine: Chlor-Trimeton, and generics

Dexchlorpheniramine: various generics

**Antihistamine**

No



No



3



C/B

**CHLORPHENIRAMINE MALEATE:**

Tabs [OTC]: 4 mg

Caplets: 8 mg

Chewable tab [OTC]: 2 mg

Sustained-release tabs [OTC]: 12 mg

Syrup [OTC]: 2 mg/5 mL (473 mL); may contain 5% alcohol and/or parabens

**DEXCHLORPHENIRAMINE MALEATE:**

Syrup: 2 mg/5 mL (473 mL); may contain alcohol

Sustained-release tabs: 6 mg

**CHLORPHENIRAMINE MALEATE DOSING:***Child < 12 yr:* 0.35 mg/kg/24 hr PO ÷ Q4–6 hr or dose based on age as follows:*2–5 yr:* 1 mg/dose PO Q4–6 hr; **max. dose** 6 mg/24 hr*6–11 yr:* 2 mg/dose PO Q4–6 hr; **max. dose** 12 mg/24 hr*≥12 yr–adult:* 4 mg/dose Q4–6 hr PO; **max. dose** 24 mg/24 hr*Sustained-release:* 12 mg PO Q12 hr**DEXCHLORPHENIRAMINE MALEATE DOSING:***Immediate-release product:**2–5 yr:* 0.5 mg/dose PO Q4–6 hr; **max. dose** 3 mg/24 hr*6–11 yr:* 1 mg/dose PO Q4–6 hr; **max. dose** 6 mg/24 hr*≥12 yr–adult:* 2 mg/dose PO Q4–6 hr; **max. dose** 12 mg/24 hr*Sustained-release product:**≥12 yr–adult:* 6 mg PO QHS or Q8–10 hr; **max. dose** 12 mg/24 hr**Use with caution** in asthma. May cause sedation, dry mouth, blurred vision, urinary retention, polyuria, and disturbed coordination. Young children may be paradoxically excited.Combination over-the-counter (OTC or nonprescription) cough and cold products are **not recommended** for children <age 6; serious adverse effects (cardiac and respiratory distress, convulsions, and hallucinations) and fatalities (from unintentional overdoses, including combined use of other OTC products containing the same active ingredients) have been reported.**NOTE:** Dexchlorpheniramine maleate doses are 50% of chlorpheniramine maleate and do not possess any significant advantages over other antihistamines.Doses may be administered PRN. Administer doses with food. Sustained-release forms are **NOT recommended** in children <6 yr and should **NOT** be crushed, chewed, or dissolved.

Pregnancy category is “C” for chlorpheniramine and “B” for dexchlorpheniramine.

**CHLORPROMAZINE**

Thorazine and generics

**Antiemetic, antipsychotic, phenothiazine derivative**

No



No



3



C

Tabs: 10, 25, 50, 100, 200 mg

Injection: 25 mg/mL (1, 2 mL); contains 2% benzyl alcohol

**Psychosis:***Child > 6 mo:**PO:* 2.5–6 mg/kg/24 hr ÷ Q4–6 hr; **max. PO dose:** 500 mg/24 hr*IM/IV:* 2.5–4 mg/kg/24 hr ÷ Q6–8 hr

CHLORPROMAZINE *continued***Max. IM/IV dose:**

&lt;5 yr: 40 mg/24 hr

5–12 yr: 75 mg/24 hr

**Adult:****PO:** 10–25 mg/dose Q4–6 hr; **max. dose** 2 g/24 hr**IM/IV:** Initial, 25 mg; if needed, repeat with 25–50 mg/dose Q1–4 hr up to a **max. dose** of 400 mg/dose Q4–6 hr**Antiemetic:****Child (≥6 mo):****IV/IM/PO:** 0.5–1 mg/kg/dose Q6–8 hr PRN**Max. IM/IV/PO dose:**

&lt;5 yr: 40 mg/24 hr

5–12 yr: 75 mg/24 hr

**Adult:****IV/IM:** 25–50 mg/dose Q4–6 hr PRN**PO:** 10–25 mg/dose Q4–6 hr PRN

Adverse effects include drowsiness, jaundice, lowered seizure threshold, extrapyramidal/anticholinergic symptoms, hypotension (more with IV), arrhythmias, agranulocytosis, and neuroleptic malignant syndrome. May potentiate effect of narcotics, sedatives, and other drugs. Monitor BP closely. ECG changes include prolonged PR interval, flattened T waves, and ST depression; do not use in combination with fluoxetine, haloperidol, citalopram, and other drugs that can prolong QT interval. **Do not administer oral liquid dosage form simultaneously with carbamazepine oral suspension;** an orange rubbery precipitate may form.

**CHOLECALCIFEROL**

D-3, D3-5, D3-50, D Drops, Enfamil D-Vi-Sol, and many others

**Vitamin D<sub>3</sub>**

No



No



2



A/D

**Tablet [OTC]:** 400, 1000, 2000, 3000, 5000, 25,000 IU**Softgel caps [OTC]:** 1000, 2000, 4000, 5000, 10,000, 25,000 IU**Caps:** 1000, 2000, 5000 IU**D3–5:** 5000 IU**D3–50:** 50,000 IU**Oral drops (D Drops) [OTC]:** 400, 1000, 2000 IU/drop (10 mL)**Oral liquid:** (Enfamil D-Vi-Sol): 400 IU/mL (50 mL)**Dietary supplementation (see Chapter 21 for additional information):****Preterm:** 400–800 IU/24 hr PO**Infant (<1 yr):** 400 IU/24 hr PO**Breast-fed neonate and infant:** 400 IU/24 hr PO**Child (≥1 yr) and adolescent:** 600 IU/24 hr PO

**Vitamin D deficiency and/or rickets (with calcium and phosphorus supplementation; decrease dose (all ages) to 400 IU once daily when radiologically proven healing is achieved):**

&lt;1 mo: 1000 IU/24 hr PO × 2–3 mo

1–12 mo: 1000–5000 IU/24 hr PO × 2–3 mo

&gt;12 mo: 5000–10,000 IU/24 hr PO × 2–3 mo

*Continued*

CHOLECALCIFEROL *continued*

**Renal failure (CKD stages 2–5) and 25-OH vitamin D levels  $\leq 30$  ng/mL (monitor serum 25-OH vitamin D and corrected calcium/phosphorus one month after initiation and Q3 mo thereafter):**

**Child (PO):**

**25-OH vitamin D  $< 5$  ng/mL:** 8000 IU/24 hr  $\times$  4 wk, followed by 4000 IU/24 hr  $\times$  2 mo; **OR** 50,000 IU weekly  $\times$  4 wk, followed by 50,000 IU twice monthly for 3 mo

**25-OH vitamin D 5–15 ng/mL:** 4000 IU/24 hr  $\times$  12 wk; **OR** 50,000 IU every other wk  $\times$  12 wk

**25-OH vitamin D 16–30 ng/mL:** 2000 IU/24 hr  $\times$  3 mo; **OR** 50,000 IU monthly  $\times$  3 mo

**Maintenance dose (after repletion):** 200–1000 IU once daily

Biological potency and oral absorption may be greater than ergocalciferol (vitamin D<sub>2</sub>).

Requires activation by the liver (25-hydroxylation) and kidney (1-hydroxylation) to the active form, calcitriol.



**Monitor** serum Ca<sup>2+</sup>, PO<sub>4</sub>, 25-OH vitamin D (goal level for infant and child:  $\geq 20$  ng/mL) and alkaline phosphate. Serum Ca<sup>2+</sup>, PO<sub>4</sub> product should be  $< 70$  mg/dL to avoid ectopic calcification. Serum 25-OH vitamin D level of  $\geq 35$  ng/mL has been used in cystic fibrosis patients to decrease risk of hyperparathyroidism and bone loss.

Toxic effects in infants may result in nausea, vomiting, constipation, abdominal pain, loss of appetite, polydipsia, polyuria, muscle weakness, muscle/joint pain, confusion, and fatigue; renal damage may also occur.

Pregnancy category changes to “D” if used in doses above the U.S. RDA.

**CHOLESTYRAMINE**

Questran, Questran Light, Cholestyramine Light, Prevalite, and generics

**Antilipemic, binding resin**



No



No



2



C

**Powder for oral suspension:**

Questran and generics: 4 g anhydrous resin per 9 g powder (9, 378 g)

Questran Light: 4 g anhydrous resin per 6.4 g powder with aspartame (210, 239 g)

Cholestyramine Light: 4 g anhydrous resin per 5.7 g powder with aspartame (210, 239 g)

Prevalite: 4 g anhydrous resin per 5.5 g powder with aspartame (5.5, 231 g)

**All doses based in terms of anhydrous resin. Titrate dose based on response and tolerance.**

**Child:** 240 mg/kg/24 hr  $\div$  TID; doses normally **do not exceed** 8 g/24 hr (higher doses do not provide additional benefit). Give PO as slurry in water, juice, or milk before meals.

**Adult:** 3–4 g of cholestyramine BID–QID; **max. dose** 24 g/24 hr.



In addition to the use for managing hypercholesterolemia, drug may be used for itching associated with elevated bile acids and diarrheal disorders associated with excess fecal bile acids or *Clostridium difficile* (pseudomembranous colitis). May also be applied topically for diaper dermatitis by preparing a 5% or 10% topical product with hydrophilic topical ointment (Aquaphor); other compounded topical formulations exist (e.g., Butt paste: cholestyramine, sucralfate, zinc oxide, and Eucerin).



May cause constipation, abdominal distention, vomiting, vitamin deficiencies (A, D, E, K), and rash. Hyperchloremic acidosis may occur with prolonged use.

Give other oral medications 4–6 hr after cholestyramine or 1 hr before dose to avoid decreased absorption.

**CHOLINE MAGNESIUM TRISALICYLATE**

Trilisate and generics

**Nonsteroidal anti-inflammatory agent**

No



Yes



?



C/D

Combination of choline salicylate and magnesium salicylate (1:1.24 ratio, respectively); strengths expressed in terms of mg salicylate:

**Tabs:** 500, 750, 1000 mg

**Oral liquid:** 500 mg/5 mL (240 mL)

**Dose based on total salicylate content.**

**Child:** 30–60 mg/kg/24 hr PO ÷ TID–QID

**Adult:** 500 mg–1.5 g/dose PO once daily–TID



**Avoid use** in patients with suspected varicella or influenza, owing to concerns of Reye syndrome.

**Use with caution** in severe renal failure because of risk for hypermagnesemia, or in peptic ulcer disease. Less GI irritation than aspirin and other NSAIDs. No antiplatelet effects.

Pregnancy category changes to “D” if used during the third trimester.

Therapeutic salicylate levels, see *Aspirin*. 500 mg choline magnesium trisalicylate is equivalent to 650 mg aspirin.

**CICLESONIDE**

Alvesco, Omnaris, Zetonna

**Corticosteroid**

Yes



No



2



C

**Aerosol inhaler (Alvesco):** 80 mcg/actuation (6.1 g = 60 doses), 160 mcg/actuation (6.1 g = 60 doses)

**Nasal spray:**

**Omnaris (nasal suspension):** 50 mcg/actuation (12.5 g = 120 doses)

**Zetonna (nasal aerosol solution):** 37 mcg/actuation (6.1 g = 60 doses)

**Intranasal (allergic rhinitis):**

**Omnaris:**

**2–11 yr (limited data):** 1–2 sprays (50–100 mcg) per nostril once daily. **Max. dose:** 200 mcg/24 hr. 2 sprays (100 mcg) per nostril once daily is approved for use in children ≥6 yr for seasonal allergic rhinitis.

**≥12 yr and adult:** 2 sprays (100 mcg) per nostril once daily. **Max. dose:** 200 mcg/24 hr.

**Zetonna:**

**≥12 yr and adult:** 1 spray (37 mcg) per nostril once daily. **Max. dose:** 74 mcg/24 hr.

**Oral inhalation (asthma):**

**≥5 yr and adult (limited data; see below for current FDA-labeled dosage information):** The following regimen has been suggested by the Global Strategy for Asthma Management and Prevention):

**Low dose:** 80–160 mcg/24 hr

**Medium dose:** >160–320 mcg/24 hr

**High dose:** >320 mcg/24 hr up to a **maximum** of 640 mcg/24 hr

**≥12 yr and adult:**

**Prior use with bronchodilator only:** 80 mcg/dose BID; **max. dose** 320 mcg/24 hr

**Prior use with inhaled corticosteroid:** 80 mcg/dose BID; **max. dose** 640 mcg/24 hr

**Prior use with oral corticosteroid:** 320 mcg/dose BID; **max. dose** 640 mcg/24 hr



Continued

CICLESONIDE *continued*

Ciclesonide is a prodrug hydrolyzed to an active metabolite, des-ciclesonide, via esterases in nasal mucosa and lungs; further metabolism is via hepatic CYP 3A4 and 2D6. Concurrent use with ketoconazole and other CYP 450 3A4 inhibitors may increase systemic des-ciclesonide levels. **Use with caution** and monitor in hepatic impairment.

**Oral inhalation (asthma):** Rinse mouth after each use. May cause headache, arthralgia, nasal congestion, nasopharyngitis, and URIs. Maximum benefit may not be achieved until 4 wk after initiation; consider dose increase if response is inadequate 4 wk after initial dosage.

**Intranasal (allergic rhinitis):** Clear nasal passages prior to use. May cause otalgia, epistaxis, nasopharyngitis, and headache. Monitor linear growth of pediatric patients routinely. Onset of action: 24–48 hours; further improvement observed over 1–2 wk in seasonal allergic rhinitis or 5 wk in perennial allergic rhinitis.

**CIDOFOVIR**

Vistide and generics

**Antiviral**

No



Yes



3



C

**Injection:** 75 mg/mL (5 mL); preservative free

**Safety and efficacy has not been established in children.**

**CMV retinitis:**

**Adult:**

**Induction:** 5 mg/kg IV once weekly  $\times$  2 with probenecid and hydration

**Maintenance:** 5 mg/kg IV Q2 wk with probenecid and hydration

**Adenovirus infection in immunocompromised oncology patients (limited data; see remarks):**

**Child:** 5 mg/kg/dose IV once weekly until PCR negative. Administer oral probenecid 1–1.25 g/m<sup>2</sup>/dose (rounded to the nearest 250-mg interval) 3 hr before and 1 hr and 8 hr after each dose of cidofovir. Also give IV normal saline at 3 times maintenance fluid 1 hr before and 1 hr after cidofovir, followed by 2 times maintenance fluid for an additional 2 hr. For patients with renal dysfunction (see remarks), give 1 mg/kg/dose IV 3 times weekly until PCR negative.

**BK virus hemorrhagic cystitis (limited data):** 1 mg/kg/dose IV once weekly without probenecid.

**Contraindicated** in hypersensitivity to probenecid or sulfa-containing drugs; sCr > 1.5 mg/dL, CrCl  $\leq$  55 mL/min, urine protein  $\geq$  100 mg/dL (2+ proteinuria), direct intraocular injection of cidofovir, and concomitant nephrotoxic drugs. **Renal impairment is the major dose-limiting toxicity.** IV NS prehydration and probenecid must be used (unless not indicated) to reduce risk of nephrotoxicity. May also cause nausea, vomiting, headache, rash, metabolic acidosis, uveitis, decreased intraocular pressure, and neutropenia.

Reported criteria for defining renal dysfunction in children include sCr > 1.5 mg/dL, GFR < 90 mL/min/1.73 m<sup>2</sup>, and >2+ proteinuria. For adults, reduce dose to 3 mg/kg if sCr increases 0.3–0.4 mg/dL from baseline. Discontinue therapy if sCr increases  $\geq$  0.5 mg/dL from baseline or with development of  $\geq$  3+ proteinuria.

Administer doses via IV infusion over 1 hr at a concentration  $\leq$  8 mg/mL.

**CIMETIDINE**

Tagamet, Tagamet HB [OTC], and generics

**Histamine-2 antagonist**

Yes



Yes



2



B

**Tabs:** 200 [OTC], 300, 400, 800 mg**Oral solution:** 300 mg/5 mL (240 mL); may contain 2.8% alcohol**Neonate:** 5–20 mg/kg/24 hr PO ÷ Q6–12 hr**Infant:** 10–20 mg/kg/24 hr PO ÷ Q6–12 hr**Child:** 20–40 mg/kg/24 hr PO ÷ Q6 hr**Adult:** 300 mg/dose PO QID **OR** 400 mg/dose PO BID **OR** 800 mg/dose PO QHS**Ulcer prophylaxis:** 400–800 mg PO QHS

Diarrhea, rash, myalgia, confusion, neutropenia, gynecomastia, elevated liver function tests, or dizziness may occur. **Use with caution** in hepatic and renal impairment (**adjust dose in renal failure; see Chapter 31**).



Inhibits CYP 450 1A2, 2C9, 2C19, 2D6, 2E1, and 3A4 isoenzymes; therefore increases levels and effects of many hepatically metabolized drugs (i.e., theophylline, phenytoin, lidocaine, diazepam, warfarin). Cimetidine may decrease absorption of iron, ketoconazole, and tetracyclines.

**CIPROFLOXACIN**

Cipro, Cipro XR, Ciloxan ophthalmic, Cetraxal, Ciprodex, Cipro HC Otic, and generics

**Antibiotic, quinolone**

No



Yes



2



C

**Tabs:** 100, 250, 500, 750 mg**Extended-release tabs (Cipro XR):** 500, 1000 mg**Oral suspension:** 250 mg/5 mL (100 mL), 500 mg/5 mL (100 mL)**Injection:** 10 mg/mL (40 mL)**Premixed injection:** 200 mg/100 mL 5% dextrose, 400 mg/100 mL 5% dextrose (iso-osmotic solutions)**Ophthalmic solution:** 3.5 mg/mL (2.5, 5, 10 mL)**Ophthalmic ointment:** 3.3 mg/g (3.5 g)**Otic suspension:****Cetraxal:** 0.5 mg/0.25 mL (14s)**With dexamethasone (Ciprodex):** 3 mg/mL ciprofloxacin + 1 mg/mL dexamethasone (7.5 mL); contains benzalkonium chloride**With hydrocortisone (Cipro HC Otic):** 2 mg/mL ciprofloxacin + 10 mg/mL hydrocortisone (10 mL); contains benzyl alcohol**Child:****PO:** 20–30 mg/kg/24 hr ÷ Q12 hr; **max. dose** 1.5 g/24 hr**IV:** 20–30 mg/kg/24 hr ÷ Q12 hr; **max. dose** 800 mg/24 hr**Complicated UTI or pyelonephritis (×10–21 days):****PO:** 20–40 mg/kg/24 hr ÷ Q12 hr; **max. dose** 1.5 g/24 hr**IV:** 18–30 mg/kg/24 hr ÷ Q8 hr; **max. dose** 1.2 g/24 hr**Cystic fibrosis:****PO:** 40 mg/kg/24 hr ÷ Q12 hr; **max. dose** 2 g/24 hr**IV:** 30 mg/kg/24 hr ÷ Q8 hr; **max. dose** 1.2 g/24 hr**Anthrax (see remarks):****Inhalational/systemic/cutaneous:** Start with 20–30 mg/kg/24 hr ÷ Q12 hr IV (**max. dose** 800 mg/24 hr) and convert to oral dosing with clinical improvement at 20–30 mg/kg/24 hr ÷ Q12 hr PO (**max. dose** 1 g/24 hr). Duration of therapy: 60 days (IV and PO combined)

Continued



CIPROFLOXACIN *continued***Child:**

**Postexposure prophylaxis:** 20–30 mg/kg/24 hr ÷ Q12 hr PO × 60 days; **max. dose** 1 g/24 hr

**Adult:****PO:**

**Immediate-release:** 250–750 mg/dose Q12 hr

**Extended-release (Cipro XR):**

**Uncomplicated UTI/cystitis:** 500 mg/dose Q24 hr

**Complicated UTI/uncomplicated pyelonephritis:** 1000 mg/dose Q24 hr

**IV:** 200–400 mg/dose Q12 hr; 400 mg/dose Q8 hr for more severe/complicated infections

**Anthrax (see remarks):**

**Inhalational/systemic/cutaneous:** Start with 400 mg/dose Q12 hr IV, and convert to oral dosing with clinical improvement at 500 mg/dose Q12 hr PO. Duration of therapy: 60 days (IV and PO combined).

**Postexposure prophylaxis:** 500 mg/dose Q12 hr PO × 60 days.

**Ophthalmic solution:**

**≥ 1 yr and adult:** 1–2 drops Q2 hr while awake × 2 days, then 1–2 drops Q4 hr while awake × 5 days

**Ophthalmic ointment:**

**≥ 2 yr and adult:** Apply 0.5-inch ribbon TID × 2, then BID × 5 days

**Otic:****Cetraxal:**

**Acute otitis externa (≥ 1 yr and adult):** 0.25 mL to affected ear(s) BID × 7 days

**Ciprodex:**

**Acute otitis media with tympanostomy tubes or acute otitis externa (≥ 6 mo and adult):** 4 drops to affected ear(s) BID × 7 days

**Cipro HC Otic:**

**Otitis externa (> 1 yr and adult):** 3 drops to affected ear(s) BID × 7 days

Can cause GI upset, renal failure, and seizures. GI symptoms, headache, restlessness, and rash are common side effects. Peripheral neuropathy has been reported.



**Use with caution** in children <18 yr (like other quinolones, tendon rupture can occur during or after therapy, especially with concomitant corticosteroid use), alkalinized urine (crystalluria), seizures, excessive sunlight (photosensitivity), and renal dysfunction (**adjust systemic dose in renal failure; see Chapter 31**). **Do not use otic suspension with perforated tympanic membranes and with viral infections of the external ear canal.**

For dosing in obese patients, use an adjusted body weight (ABW).  $ABW = \text{Ideal body weight} + 0.45 (\text{Total body weight} - \text{Ideal body weight})$ .

Combinational antimicrobial therapy is recommended for anthrax. For penicillin-susceptible strains, consider changing to high-dose amoxicillin (25–35 mg/kg/dose TID PO). See [www.bt.cdc.gov](http://www.bt.cdc.gov) for the latest information.

Inhibits CYP 450 1A2. Ciprofloxacin can increase effects and/or toxicity of caffeine, methotrexate, theophylline, warfarin, tizanidine (excessive sedation and dangerous hypotension), and cyclosporine. Probenecid increases ciprofloxacin levels.

**Do not administer antacids or other divalent salts** with or within 2–4 hr of oral ciprofloxacin dose.

**CITRATE MIXTURES***Alkalinizing agent, electrolyte supplement*

No



Yes



?



?

Each mL of oral solution contains the following mEq of electrolyte:

	Na	K	Citrate or HCO <sub>3</sub>
Tricitrates* (480 mL)	1	1	2
Cytra-K*† (480 mL)	0	2	2
Cytra-2* or Sodium Citrate/Citric Acid* (480 mL)	1	0	1
Oracit (15, 30, 500 mL)	1	0	1

\*Sugar-free

†Also available as a powder for oral solution; each packet of powder must be diluted before use and contains 30 mEq each of potassium and citrate/HCO<sub>3</sub> (100 packets per box)**Dilute dose in water or juice.****All mEq doses based on citrate.****Infant and child (PO):** 2–3 mEq/kg/24 hr ÷ Q6–8 hr or 5–15 mL/dose Q6–8 hr (after meals and before bedtime)**Adult (PO):** 100–200 mEq/24 hr ÷ Q6–8 hr or 15–30 mL/dose Q6–8 hr (after meals and before bedtime)**Contraindicated** in severe renal impairment and acute dehydration. **Use with caution** in patients already receiving potassium supplements or who are sodium restricted. May have laxative effect and cause hypocalcemia and metabolic alkalosis.Adjust dose to maintain desired pH. 1 mEq of citrate is equivalent to 1 mEq HCO<sub>3</sub> in patients with normal hepatic function.**CLARITHROMYCIN**

Biaxin, Biaxin XL, and generics

*Antibiotic, macrolide*

Yes



Yes



2



C

**Film tablets:** 250, 500 mg**Extended-release tablets (Biaxin XL):** 500 mg**Granules for oral suspension:** 125, 250 mg/5 mL (50, 100 mL)**Infant and child:****Acute otitis media, pharyngitis/tonsillitis, pneumonia, acute maxillary sinusitis, or uncomplicated skin infections:** 15 mg/kg/24 hr PO ÷ Q12 hr; **max. dose** 1 g/24 hr**Pertussis (≥ 1 mo):** 15 mg/kg/24 hr PO ÷ Q12 hr × 7 days; **max. dose** 1 g/24 hr**Bacterial endocarditis prophylaxis:** 15 mg/kg (**max. dose** 500 mg) PO 1 hr before procedure**Mycobacterium avium complex (MAC):****Prophylaxis (1st episode and recurrence):** 15 mg/kg/24 hr PO ÷ Q12 hr**Treatment:** 15 mg/kg/24 hr PO ÷ Q12 hr with other antimycobacterial drugs**Max. dose:** 1 g/24 hr**Adolescent and adult:****Pharyngitis/tonsillitis, acute maxillary sinusitis, bronchitis, pneumonia, or uncomplicated skin infections:****Immediate-release:** 250–500 mg/dose Q12 hr PO**Extended-release (Biaxin XL):** 1000 mg Q24 hr PO (currently not indicated for pharyngitis/tonsillitis or uncomplicated skin infections)

Continued

CLARITHROMYCIN *continued***Adult:****Pertussis:** 500 mg (immediate-release)/dose Q12 hr PO  $\times$  7 days**Bacterial endocarditis prophylaxis:** 500 mg PO 1 hr before procedure**MAC:****Prophylaxis (1st episode and recurrence):** 500 mg/dose Q12 hr PO**Treatment:** 500 mg Q12 hr PO with other antimycobacterial drugs**Helicobacter pylori GI infection:** 250 mg Q12 hr to 500 mg Q8 hr PO with omeprazole or ranitidine and bismuth; or amoxicillin and omeprazole or lansoprazole.

**Contraindicated** in patients allergic to erythromycin and history of cholestatic jaundice/hepatic dysfunction with prior use. As with other macrolides, clarithromycin has been associated with QT prolongation and ventricular arrhythmias, including ventricular tachycardia and torsades de pointes. May cause cardiac arrhythmias in patients also receiving cisapride. Side effects: diarrhea, nausea, abnormal taste, dyspepsia, abdominal discomfort (less than erythromycin but greater than azithromycin), and headache. Rare cases of anaphylaxis, hepatic dysfunction, rhabdomyolysis, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported. May increase effects/toxicity of carbamazepine, theophylline, cyclosporine, digoxin, ergot alkaloids, fluconazole, tacrolimus, triazolam, and warfarin. Substrate and inhibitor of CYP 450 3A4, and inhibits CYP 1A2.



**Adjust dose in renal failure (see Chapter 31).** Doses, regardless of dosage form, may be administered with food.

**CLINDAMYCIN**

Cleocin-T, Cleocin, and generics

**Antibiotic, lincomycin derivative**

Yes



Yes



2



B

**Caps:** 75, 150, 300 mg**Oral solution:** 75 mg/5 mL (100 mL)**Injection:** 150 mg/mL (contains 9.45 mg/mL benzyl alcohol)**Premixed injection in 5% dextrose:** 300 mg/50 mL, 600 mg/50 mL, 900 mg/50 mL**Solution, topical (Cleocin-T):** 1% (30, 60 mL); may contain 50% isopropyl alcohol**Gel, topical (Cleocin-T):** 1% (30, 60 g); may contain methylparaben**Lotion, topical (Cleocin-T):** 1% (60 mL); may contain methylparaben**Foam, topical:** 1% (50, 100 g); contains 58% ethanolSee *Benzoyl Peroxide* for combination topical product (clindamycin and benzoyl peroxide)**Vaginal cream:** 2% (40 g); may contain benzyl alcohol**Vaginal suppository:** 100 mg (3s)**Neonate:****IV/IM:** 5 mg/kg/dose with the following dosage intervals: **$\leq 7$  days:** **$\leq 2$  kg:** Q12 hr **$> 2$  kg:** Q8 hr **$> 7$  days:** **$< 1.2$  kg:** Q12 hr **$1.2$ – $2$  kg:** Q8 hr **$> 2$  kg:** Q6 hr**Child:****PO:** 10–30 mg/kg/24 hr  $\div$  Q6–8 hr; **max. dose** 1.8 g/24 hr**IM/IV:** 25–40 mg/kg/24 hr  $\div$  Q6–8 hr; **max. dose** 4.8 g/24 hr

CLINDAMYCIN *continued***Child:**

**Bacterial endocarditis prophylaxis:** 20 mg/kg (**max. dose** 600 mg)  $\times$  1 PO or IV; 1 hr before procedure with PO route and 30 min before procedure with IV route.

**Adult:**

**PO:** 150–450 mg/dose Q6–8 hr; **max. dose** 1.8 g/24 hr

**IM/IV:** 1200–1800 mg/24 hr IM/IV  $\div$  Q6–12 hr; **max. dose** 4.8 g/24 hr

**Bacterial endocarditis prophylaxis:** 600 mg  $\times$  1 PO or IV; 1 hr before procedure with PO route and 30 min before procedure with IV route.

**Topical ( $\geq$  12 yr and adult):** apply to affected area BID.

**Bacterial vaginosis (adolescent and adult):**

**Suppositories:** 100 mg/dose QHS  $\times$  3 days

**Vaginal cream (2%):** 1 applicator dose (5 g) QHS for 3 or 7 days in nonpregnant patients and for 7 days in pregnant patients in second and third trimesters.

Not indicated in meningitis; CSF penetration is poor.

Pseudomembranous colitis may occur up to several weeks after cessation of therapy. May cause diarrhea, rash, Stevens-Johnson syndrome, granulocytopenia, thrombocytopenia, or sterile abscess at injection site.



Clindamycin may increase the neuromuscular blocking effects of tubocurarine, pancuronium. **Do not exceed** IV infusion rate of 30 mg/min; hypotension, cardiac arrest has been reported with rapid infusions.

Dosage reduction may be required in severe renal or hepatic disease but not necessary in mild/moderate conditions. Oral liquid preparation may not be palatable; consider use of oral capsules as a sprinkle onto applesauce or pudding.

**CLOBAZAM**

Onfi

**Benzodiazepine, anticonvulsant**



Yes



No



3



C

**Tabs:** 10, 20 mg

**Oral suspension:** 2.5 mg/mL (120 mL); contains parabens, polysorbate 80 and propylene glycol

**Lennox-Gastaut (adjunctive therapy (see remarks)):**

**Child ( $\geq$  2 yr) and adult (PO):** Dosage increments (if needed) should not be more rapid than Q7 days.



Weight (kg)	Initial Dose	Dose at Day 8 (if needed)	Dose at Day 15 (if needed)
$\leq$ 30 kg	5 mg once daily	5 mg BID	10 mg BID ( <b>max. dose</b> )
$>$ 30 kg	5 mg BID	10 mg BID	20 mg BID ( <b>max. dose</b> )

**Dosage adjustment for mild/moderate hepatic impairment (Child-Pugh score 5–9) and individuals with poor CYP 450 2C19 activity (PO):**

Weight (kg)	Initial Dose	First Dose Increment (if needed)	Second Dose Increment (if needed)	Third Dose Increment (if needed)
$\leq$ 30 kg	5 mg once daily $\times \geq$ 14 days	5 mg BID $\times \geq$ 7 days	10 mg BID ( <b>max. dose</b> )	N/A
$>$ 30 kg	5 mg once daily $\times \geq$ 7 days	5 mg BID $\times \geq$ 7 days	10 mg BID $\times \geq$ 7 days	20 mg BID ( <b>max. dose</b> )

N/A = Not applicable.

*Continued*

CLOBAZAM *continued*

**Seizures (generalized or partial, as monotherapy or adjunctive therapy; limited data and prescribing information from Canada and the UK):**

**Infant and child (<2 yr):** Start at 0.5–1 mg/kg/24 hr (**max. dose** 5 mg/24 hr) PO ÷ BID; if needed and tolerated, slowly increase dosage at 5–7 day intervals up to the **maximum** of 10 mg/kg/24 hr.  
**2–16 yr:** Start at 5 mg PO once daily; if needed and tolerated, slowly increase dosage at 5–7 day intervals up to the **maximum** of 40 mg/kg/24 hr. Usual dosage range: 10–20 mg/24 hr or 0.3–1 mg/kg/24 hr ÷ BID.

**Use with caution** in hepatic impairment (dose adjustment may be needed). **Do not discontinue use abruptly** because seizures/withdrawal symptoms may occur. Common side effects include constipation, drooling, ataxia, drowsiness, insomnia, aggressive behavior, cough and fever. Stevens-Johnson syndrome, TEN, leukopenia, and thrombocytopenia have been reported.



**Do not use in combination** with azelastine, olanzapine, sodium oxybate, and thioridazine; increased risk of adverse events. Proton-pump inhibitors, azole antifungal agents (e.g., itraconazole, ketoconazole), St. John's wort, grapefruit juice, CNS depressants, cimetidine, and calcium channel blockers may increase the effects/toxicity of clobazam. Carbamazepine, rifamycin derivatives (e.g., rifampin), and theophylline may decrease the effects of clobazam. Clobazam is a major substrate for CYP 450 2C19 and P-glycoprotein, minor substrate for CYP 450 2B6 and 3A4, inhibitor of CYP 450 2D6, and inducer of CYP 3A4. Carefully review patient's medication profile for other drug interactions each time clobazam is initiated or when a new drug is added to a regimen containing clobazam.

Doses may be taken with or without food. Tablets may be crushed and mixed with applesauce.

**CLONAZEPAM**

Klonopin and others

**Benzodiazepine, anticonvulsant**



Yes



Yes




3



D

**Tabs:** 0.5, 1, 2 mg

**Disintegrating oral tabs:** 0.125, 0.25, 0.5, 1, 2 mg; contains phenylalanine

**Oral suspension:** 100 mcg/mL 

**Infant and child:** <10 yr or <30 kg:

**Initial:** 0.01–0.03 mg/kg/24 hr ÷ Q8 hr PO. **Maximum initial dose:** 0.05 mg/kg/24 hr.

**Increment:** 0.25–0.5 mg/24 hr Q3 days, up to **maximum maintenance dose** of 0.1–0.2 mg/kg/24 hr ÷ Q8 hr.

**Child ≥ 10 yr or ≥ 30 kg and adult:**

**Initial:** 1.5 mg/24 hr PO ÷ TID

**Increment:** 0.5–1 mg/24 hr Q3 days; **max. dose** 20 mg/24 hr



**Contraindicated** in severe liver disease and acute narrow-angle glaucoma. Drowsiness, behavior changes, increased bronchial secretions, GI, CV, GU, and hematopoietic toxicity (thrombocytopenia, leukopenia) may occur. Monitor for depression, suicidal behavior/ideation, and unusual changes in behavior/mood. **Use with caution** in patients with renal impairment.



**Do not discontinue abruptly.**  $T_{1/2}$ : 24–36 hr.

**Proposed therapeutic levels (not well established):** 20–80 ng/mL. Recommended serum sampling time: Obtain trough level within 30 min before an oral dose. Steady state is typically achieved after 5–8 days of continuous therapy using the same dose.

Carbamazepine, phenytoin, and phenobarbital may decrease clonazepam levels and effect. Drugs that inhibit CYP 450 3A4 isoenzymes (e.g., erythromycin) may increase clonazepam levels and effects/toxicity.

**CLONIDINE**

Catapres, Kapvay, Nexiclon XR, Catapres TTS, Duraclon, and generics

**Central  $\alpha$ -adrenergic agonist, antihypertensive**



No



No



3



C

**Tabs:** 0.1, 0.2, 0.3 mg

**Oral suspension:** 20, 100 mcg/mL

**Transdermal patch (Catapres TTS and generics):** 0.1, 0.2, 0.3 mg/24 hr (7-day patch); contains metallic components (see remarks)

**Injection, epidural (Duraclon and generics):** 100, 500 mcg/mL (10 mL); preservative free

**Extended-release oral preparations:**

**Extended-release oral tab:**

**Kapvay and generics:** 0.1, 0.2 mg; also available as dose pack blister cards, 60 tablets each of 0.1 and 0.2 mg tablets

**Nexiclon XR:** 0.17 mg; for Q24 hr dosing

**Extended-release oral liquid (Nexiclon XR):** 0.09 mg/mL (118 mL); for Q24 hr dosing

**Hypertension (use immediate-release products unless noted):**

**Child (PO):** 5–10 mcg/kg/24 hr  $\div$  Q8–12 hr initially; if needed, increase at 5–7 day intervals to 5–25 mcg/kg/24 hr  $\div$  Q6 hr; **max. dose** 25 mcg/kg/24 hr up to 0.9 mg/24 hr.

**$\geq 12$  yr and adult (PO):** 0.1 mg BID initially; increase in 0.1 mg/24 hr increments at weekly intervals until desired response is achieved (usual range: adolescent, 0.2–0.6 mg/24 hr  $\div$  BID; adult, 0.1–0.8 mg/24 hr  $\div$  BID). **Max. dose:** 2.4 mg/24 hr.

**Transdermal patch:**

**Child:** Conversion to patch only after establishing an optimal oral dose first. Use a transdermal dosage closest to the established total oral daily dose.

**Adult:** Initial 0.1 mg/24 hr patch for first wk. May increase dose by 0.1 mg/24 hr at 1–2 wk intervals PRN. Usual range: 0.1–0.3 mg/24 hr. Each patch last for 7 days. Doses  $>0.6$  mg/24 hr do not provide additional benefit.

**ADHD (Child  $\geq 6$  yr and adolescent):**

**Immediate-release product (PO):** Start with 0.05 mg QHS; if needed, increase by 0.05 mg every 3–7 days up to a **max. dose** of 0.4 mg/24 hr. Titrated doses may be divided TID–QID.

**Extended-release product (Kapvay, PO):** Start with 0.1 mg QHS; if needed, increase by 0.1 mg every 7 days by administering the dose BID up to a **maximum** of 0.4 mg/24 hr. Depending on dosage level, BID dosing should be either the same amount or with the higher dosage given at bedtime. If therapy is to be discontinued, slowly reduce dosage at  $\leq 0.1$  mg every 3 to 7 days to avoid withdrawal.

**Neonatal abstinence syndrome, adjunctive therapy (use immediate-release product; limited data):**

0.5–1 mcg/kg/dose Q4–6 hr PO; use Q6 hr interval for preterm neonates.

**Side effects:** Dry mouth, dizziness, drowsiness, fatigue, constipation, anorexia, arrhythmias, and local skin reactions with patch. May worsen sinus node dysfunction and AV block, especially for patients taking other sympatholytic drugs. **Do not abruptly discontinue;** signs of sympathetic overactivity may occur; taper gradually over  $>1$  wk.

$\beta$ -Blockers may exacerbate rebound hypertension during and after withdrawal of clonidine. If patient is receiving both clonidine and a  $\beta$ -blocker and clonidine is to be discontinued, the  $\beta$ -blocker should be withdrawn several days before tapering the clonidine. If converting from clonidine to a  $\beta$ -blocker, introduce the  $\beta$ -blocker several days after discontinuing clonidine (after taper).

Monitor heart rate when used with digitalis, calcium channel blockers, and  $\beta$ -blockers. Use with diltiazem or verapamil may result in sinus bradycardia. Use with neuroleptics may induce/exacerbate orthostatic hypotension, dizziness, and fatigue.

**$T_{1/2}$ :** 44–72 hr (neonate), 6–20 hr (adult). Onset of action (antihypertensive): 0.5–1 hr for oral route, 2–3 days for transdermal route. **Do not** use transdermal route while patient is undergoing an MRI procedure; transdermal patches contain metals and may result in serious patient burns when undergoing MRI.



**CLOTRIMAZOLE**

Lotrimin AF, Gyne-Lotrimin 3, Gyne-Lotrimin 7, and generics

**Antifungal, imidazole**

Yes



No



?



B/C

**Oral troche:** 10 mg**Cream, topical [OTC]:** 1% (15, 30, 45 g); contains benzyl alcohol**Solution, topical [OTC]:** 1% (10, 30 mL)**Lotion, topical [OTC]:** 1% (20 mL); contains benzyl alcohol**Vaginal suppository [OTC]:** 200 mg**Vaginal cream [OTC]:** 1% (45 g), 2% (21 g)**Topical:** Apply to affected skin areas BID  $\times$  4–8 wk**Vaginal candidiasis (>12 yr and adult):****Vaginal suppositories** (may be used in combination with a vaginal cream applied onto the vulva once daily or BID):100 mg/dose intravaginally QHS  $\times$  7 days *OR*200 mg/dose intravaginally QHS  $\times$  3 days**Vaginal cream:**1 applicator dose (5 g) of 1% cream intravaginally QHS  $\times$  7–14 days, or1 applicator dose of 2% cream intravaginally QHS  $\times$  3 days**Thrush:****>3 yr–adult:** Slowly dissolve (15–30 min) 1 troche in mouth 5 times/24 hr  $\times$  14 days.

May cause erythema, blistering, or urticaria with topical use. Liver enzyme elevation, nausea, and vomiting may occur with troches. **Avoid use** of condoms and diaphragms with vaginal cream or suppository; latex can be weakened. **Do not use** troches for systemic infections.

Pregnancy category is “B” for topical and vaginal dosage forms and “C” for troches.

**CODEINE**

Various generics

**Narcotic, analgesic, antitussive**

Yes



Yes



2



C/D

**Tabs:** 15, 30, 60 mg; as sulfate**Oral suspension:** 3 mg/mL **Analgesic (all doses PO PRN [see remarks]):****Child:** 0.5–1 mg/kg/dose Q4–6 hr; **max. dose** 60 mg/dose**Adult:** 15–60 mg/dose Q4–6 hr**Antitussive (all doses PO PRN [see remarks]):** 1–1.5 mg/kg/24 hr  $\div$  Q4–6 hr; alternatively dose by age:**2–5 yr:** 2.5–5 mg/dose Q4–6 hr; **max. dose** 30 mg/24 hr**6–12 yr:** 5–10 mg/dose Q4–6 hr; **max. dose** 60 mg/24 hr **$\geq$ 12 yr and adult:** 10–20 mg/dose Q4–6 hr; **max. dose** 120 mg/24 hr

Use is considered **contraindicated** by the FDA for children in the postoperative period after a tonsillectomy and/or adenoidectomy. **Do not use** in children <2 yr old as antitussive. **Use with caution** in hypersensitivity reactions to other opioids, respiratory disorders, and severe liver or renal insufficiency. Side effects: CNS and respiratory depression, constipation, cramping, hypotension, and pruritus. May be habit forming.

Many **do not recommend** the use of codeine. Codeine's analgesic effect is due to its metabolism to morphine. Nursing infants whose mothers are taking codeine and are “ultra-rapid metabolizers” (CYP 450 2D6) of codeine may have a more rapid and complete conversion to morphine. This may increase the risk for morphine overdose to the nursing infant. Morphine overdose is also possible for individuals taking codeine and who are CYP 450 2D6 ultra-rapid metabolizers. See Chapter 6 for additional remarks.

Pregnancy risk factor changes to a “D” if used for prolonged periods or in high doses at term.

**CORTICOTROPIN**

Acthar HP

**Adrenocorticotrophic hormone**

No



No



?



C

**Injection, repository gel:** 80 U/mL (5 mL); contains phenol

1 unit = 1 mg

**Infantile spasms** (many regimens exist):20–40 U/24 hr IM once daily  $\times$  6 wk or 150 U/m<sup>2</sup>/24 hr  $\div$  BID for 2 wk, followed by a gradual taper**Anti-inflammatory:** $\geq 2$  yr and adolescent: 0.8 U/kg/24 hr  $\div$  Q12–24 hr IM**Contraindicated** in acute psychoses, CHF, Cushing disease, TB, peptic ulcer, ocular herpes, fungal infections, recent surgery, and sensitivity to porcine products. **Repository gel dosage form is only for IM route.**

Hypersensitivity reactions may occur. Similar adverse effects as corticosteroids.

**CORTISONE ACETATE**

Various generics

**Corticosteroid**

No



No



?



C/D

**Tabs:** 25 mg**Anti-inflammatory immunosuppressive:****Child:** 2.5–10 mg/kg/24 hr  $\div$  Q6–8 hr PO**Adult:** 25–300 mg/24 hr  $\div$  Q12–24 hr PO

May produce glucose intolerance, Cushing syndrome, edema, hypertension, adrenal suppression, cataracts, hypokalemia, skin atrophy, peptic ulcer, osteoporosis, and growth suppression.



Pregnancy category changes to “D” if used in the first trimester.

**CO-TRIMOXAZOLE**

See SULFAMETHOXAZOLE AND TRIMETHOPRIM

**CROMOLYN**

Nasal crom, Gastrocrom, Crolom, Opticrom, and various generics; previously available as Intal

**Antiallergic agent, mast cell stabilizer**

Yes



Yes



1



B

**Nebulized solution:** 10 mg/mL (2 mL)**Oral concentrate (Gastrocrom and generics):** 100 mg/5 mL**Ophthalmic solution (Crolom, Opticrom and generics):** 4% (10 mL)**Nasal spray (Nasal crom and generics) [OTC]:** 4% (5.2 mg/spray) (100 sprays, 13 mL; 200 sprays, 26 mL); contains benzalkonium chloride and EDTA**Nebulization:****Child  $\geq 2$  yr and adult:** 20 mg Q6–8 hr**Exercise-induced asthma:** 20 mg  $\times$  1, 10–15 min before and no longer than 1 hr before exercise**Nasal:****Child  $\geq 2$  yr and adult:** 1 spray each nostril TID–QID; **max. dose** 1 spray 6 times/24 hr**Ophthalmic:****Child  $> 4$  yr and adult:** 1–2 drops 4–6 times/24 hr

Continued



CROMOLYN *continued***Food allergy/inflammatory bowel disease:**2–12 yr: 100 mg PO QID; give 15–20 min AC and QHS; **max. dose** 40 mg/kg/24 hr

&gt;12 yr and adult: 200–400 mg PO QID; give 15–20 min AC and QHS

**Systemic mastocytosis:**Infant and child < 2 yr: 20 mg/kg/24 hr ÷ QID PO; **max. dose** 30 mg/kg/24 hr2–12 yr: 100 mg PO QID; give 30 min AC and QHS; **max. dose** 40 mg/kg/24 hr>12 yr and adult: 200 mg PO QID; give 30 min AC and QHS; **max. dose** 40 mg/kg/24 hr

May cause rash, cough, bronchospasm, and nasal congestion. May cause headache, diarrhea with oral use. **Use with caution** in patients with renal or hepatic dysfunction.

Therapeutic response (PO route) often occurs within 2 wk, but a 4–6 wk trial may be needed to determine maximum benefit. Oral concentrate can only be diluted in water. Nebulized solution can be mixed with albuterol nebs.

**CYANOCOBALAMIN/VITAMIN B<sub>12</sub>**Cyanocject, Cyomin, Nascobal, Vitamin B<sub>12</sub>, and generics**Vitamin (synthetic), water-soluble**

No



No



1



A/C

**Tabs [OTC]:** 100, 250, 500, 1000 mcg**Extended-release tabs:** 1000 mcg**Sublingual tabs:** 2500 mcg**Lozenges [OTC]:** 50, 100, 250, 500 mcg**Nasal spray (Nascobal):** 500 mcg/spray (1.3 mL delivers 4 doses); contains benzalkonium chloride**Injection (Cyanocject, Cyomin):** 1000 mcg/mL (1, 10, 30 mL); some preparations may contain benzyl alcohol

Contains cobalt (4.35%)

**U.S. RDA:** See Chapter 21.**Vitamin B<sub>12</sub> deficiency, treatment:****Child (IM or deep SC):** 100 mcg/24 hr × 10–15 days**Maintenance:** At least 60 mcg/mo**Adult (IM or deep SC):** 30–100 mcg/24 hr × 5–10 days**Maintenance:** 100–200 mcg/mo**Pernicious anemia:****Child (IM or deep SC):** 30–50 mcg/24 hr for at least 14 days to a total dose of 1000–5000 mcg**Maintenance:** 100 mcg/month**Adult (IM or deep SC):** 100 mcg/24 hr × 7 days, followed by 100 mcg/dose every other day × 14 days, then 100 mcg/dose Q3–4 days until remission is complete.**Maintenance:****IM/deep SC:** 100–1000 mcg/mo**Intranasal:** 500 mcg in one nostril once weekly**Sublingual:** 1000–2000 mcg/24 hr

**Contraindicated** in optic nerve atrophy. May cause hypokalemia, hypersensitivity, pruritus, and vascular thrombosis. Pregnancy category changes to “C” if used in doses above the RDA or if administered by the intranasal route.

Prolonged use of acid-suppressing medications may reduce cyanocobalamin oral absorption.

Protect product from light. Oral route of administration is poorly absorbed and generally **not recommended** for pernicious anemia and B<sub>12</sub> deficiency. IV route of administration is **not recommended** because of more rapid elimination. See Chapter 21 for multivitamin preparations.



**CYCLOPENTOLATE**

Cyclogyl and generics

**Anticholinergic, mydriatic agent**

No



No



?



C

**Ophthalmic solution:** 0.5%, 1%, 2% (2, 5, 15 mL); may contain benzalkonium chlorideAdminister dose  $\approx$  40–50 min before examination/procedure.**Infant:** Use cyclopentolate/phenylephrine (Cyclomydril) because of lower cyclopentolate concentration and reduced risk of systemic side effects.**Child:** 1 drop of 0.5%–1% OU, followed by repeat drop, if necessary, in 5 min.**Adult:** 1 drop of 1% OU followed by another drop OU in 5 min; use 2% solution for heavily pigmented iris.

**Do not use** in narrow-angle glaucoma. May cause a burning sensation, behavioral disturbance, tachycardia, and loss of visual accommodation. Psychotic reactions and behavioral disturbances have been reported in children. To minimize absorption, apply pressure over nasolacrimal sac for at least 2 min. CNS and cardiovascular side effects are common with the 2% solution in children. **Avoid** feeding infants within 4 hr of dosing to prevent potential feeding intolerance.

**Onset of action:** 15–60 min. **Duration of action:** 6–24 hr; complete recovery of accommodation may take several days for some patients. Observe patient closely for at least 30 min after dose.

**CYCLOPENTOLATE WITH PHENYLEPHRINE**

Cyclomydril

**Anticholinergic/sympathomimetic, mydriatic agent**

No



No



?



C

**Ophthalmic solution:** 0.2% cyclopentolate and 1% phenylephrine (2, 5 mL); contains 0.1% benzalkonium chloride, EDTA and boric acidAdminister dose  $\approx$  40–50 min before examination/procedure.**Neonate–adult:** 1 drop OU Q5–10 min; **max. dose** 3 drops per eyeUsed to induce mydriasis. See *Cyclopentolate* for additional remarks.**Onset of action:** 15–60 min. **Duration of action:** 4–12 hr.**CYCLOSPORINE, CYCLOSPORINE MICROEMULSION, CYCLOSPORINE MODIFIED**

Sandimmune, Gengraf, Neoral, Restasis, and generics

**Immunosuppressant**

Yes



Yes



X



C

**CYCLOSPORINE (Sandimmune and generics):****Injection:** 50 mg/mL; contains 32.9% alcohol and 650 mg/mL polyoxyethylated castor oil**Oral solution:** 100 mg/mL (50 mL); contains 12.5% alcohol**Caps:** 25, 50, 100 mg; contains 12.8% alcohol**CYCLOSPORINE MICROEMULSION (Neoral):****Caps:** 25, 100 mg**Oral solution:** 100 mg/mL (50 mL)

Neoral products contain 11.9% alcohol

**CYCLOSPORINE MODIFIED (Gengraf):****Caps:** 25, 100 mg; contains 12.8% alcohol**Oral solution:** 100 mg/mL (50 mL): Contains castor oil**OPHTHALMIC EMULSION (Restasis):** 0.05% (0.4 mL as 30 single-use vials/box); preservative free

Continued

CYCLOSPORINE, CYCLOSPORINE MICROEMULSION,  
CYCLOSPORINE MODIFIED *continued*

**Neoral manufacturer recommends a 1:1 conversion ratio with Sandimmune. Because of its better absorption, lower doses of Neoral and Gengraf may be required. Exact dosing will vary depending on transplant type.**



**Oral:** 15 mg/kg/24 hr as a single dose given 4–12 hr pretransplantation; give same daily dose ÷ Q12–24 hr for 1–2 wk posttransplantation, then reduce by 5% per wk to 3–10 mg/kg/24 hr ÷ Q12–24 hr.

**IV:** 5–6 mg/kg/24 hr as a single dose given 4–12 hr pretransplantation; administer over 2–6 hr; give same daily dose posttransplantation until patient able to tolerate oral form.

**Ophthalmic:**

≥ 16 yr and adult: Instill one drop onto affected eye(s) Q12 hr.

May cause nephrotoxicity, hepatotoxicity, hypomagnesemia, hyperkalemia, hyperuricemia, hypertension, hirsutism, acne, GI symptoms, tremor, leukopenia, sinusitis, gingival hyperplasia, and headache. Encephalopathy, convulsions, vision and movement disturbances, and impaired consciousness have been reported, especially in liver transplant patients. Psoriasis patients previously treated with PUVA and, to a lesser extent, methotrexate or other immunosuppressive agents, UVB, coal tar, or radiation therapy are at increased risk for skin malignancies when taking Neoral or Gengraf.



Opportunistic infections and activation of latent viral infections have been reported. BK virus–associated nephropathy has been observed in renal transplant patients.

**Use caution** with concomitant use of other nephrotoxic drugs (e.g., amphotericin B, aminoglycosides, NSAIDs, tacrolimus).

Plasma concentrations increased with the use of boceprevir, telaprevir, fluconazole, ketoconazole, itraconazole, erythromycin, clarithromycin, voriconazole, nefazodone, diltiazem, verapamil, nifedipine, carvedilol, and corticosteroids. Plasma concentrations decreased with the use of carbamazepine, nafcillin, rifampin, oxcarbazepine, bosentan, phenobarbital, octreotide, and phenytoin. May increase bosentan, methotrexate, repaglinide, and anthracycline antibiotics (e.g., doxorubicin, mitoxantrone, daunorubicin) levels. Use with nifedipine may result in gingival hyperplasia. Cyclosporine is a substrate and inhibitor for CYP 450 3A4 and P-glycoprotein.

Children may require dosages 2–3 times higher than adults. Plasma half-life 6–24 hr.

Monitor trough levels (just before a dose at steady state). Steady state is generally achieved after 3–5 days of continuous dosing. Interpretation will vary based on treatment protocol and assay methodology (RIA monoclonal vs. RIA polyclonal vs. HPLC) as well as whole blood vs. serum sample. Additional monitoring and dosage adjustments may be necessary in renal and hepatic impairment or when changing dosage forms.

**For ophthalmic use:** Remove contact lens prior to use; lens may be inserted 15 min after dose administration. May be used with artificial tears but must be separated by 15 min from one another.

## CYPROHEPTADINE

Various generics; previously available as Periactin  
**Antihistamine**



Yes



No



3



B

**Tabs:** 4 mg

**Syrup:** 2 mg/5 mL (473 mL); may contain alcohol

**Antihistaminic uses:**

**Child:** 0.25 mg/kg/24 hr or 8 mg/m<sup>2</sup>/24 hr ÷ Q8–12 hr PO or by age:

**2–6 yr:** 2 mg Q8–12 hr PO; **max. dose** 12 mg/24 hr

**7–14 yr:** 4 mg Q8–12 hr PO; **max. dose** 16 mg/24 hr



CYPROHEPTADINE *continued*

**Adult:** Start with 12 mg/24 hr ÷ TID PO; dosage range, 12–32 mg/24 hr ÷ TID PO; **max. dose** 0.5 mg/kg/24 hr

**Migraine prophylaxis:** 0.25–0.4 mg/kg/24 hr ÷ BID–TID PO up to following **max. doses:**

**2–6 yr:** 12 mg/24 hr

**7–14 yr:** 16 mg/24 hr

**Adult:** 0.5 mg/kg/24 hr or 32 mg/24 hr

**Appetite stimulation (see remarks):**

**≥2 yr and adolescent:** 0.25 mg/kg/24 hr ÷ Q12 hr PO up to the following **max. dose by age:** 2–6 yr, 12 mg/24 hr; 7–14 yr, 16 mg/24 hr; ≥15 yr, 32 mg/24 hr

**Alternative dosing by age:**

**4–8 yr (limited data):** 2 mg Q8 hr PO

**>13 yr and adult:** Start with 2 mg Q6 hr PO; dose may be gradually increased to 8 mg Q6 hr over a 3-wk period.

**Contraindicated** in neonates, patients currently on MAO inhibitors, and patients suffering from asthma, glaucoma, or GI/GU obstruction. May produce anticholinergic side effects, including sedation and appetite stimulation. Consider reducing dosage with hepatic insufficiency.

Allow 4–8 wk of continuous therapy for assessing efficacy in migraine prophylaxis. For use as an appetite stimulant, a dosing cycle of 3 wk on therapy, followed by 1 wk off therapy may enhance efficacy.

**DANTROLENE**

Dantrium, Revonto, and many generics

**Skeletal muscle relaxant**



Yes



No



?



C

**Cap:** 25, 50, 100 mg

**Oral suspension:** 5 mg/mL 

**Injection (Dantrium, Revonto):** 20 mg; contains 3 g mannitol/20 mg drug

**Chronic spasticity:**

**Child:** <5 yr

**Initial:** 0.5 mg/kg/dose PO BID

**Increment:** Increase frequency to TID–QID at 4- to 7-day intervals, then increase doses by 0.5 mg/kg/dose.

**Max. dose:** 3 mg/kg/dose PO BID–QID, up to 400 mg/24 hr

**Malignant hyperthermia:**

**Prevention:**

**PO:** 4–8 mg/kg/24 hr ÷ Q6 hr × 1–2 days before surgery, with last dose administered 3–4 hr before surgery

**IV:** 2.5 mg/kg over 1 hr beginning 1.25 hr before anesthesia; additional doses PRN

**Treatment:** 1 mg/kg IV, repeat PRN to **maximum cumulative dose** of 10 mg/kg, followed by a postcrisis regimen of 4–8 mg/kg/24 hr PO ÷ Q6 hr for 1–3 days

**Contraindicated** in active hepatic disease. Monitor transaminases for hepatotoxicity. **Use with caution** with cardiac or pulmonary impairment. May cause change in sensorium, drowsiness, weakness, diarrhea, constipation, incontinence, and enuresis. Rare cardiovascular collapse has been reported in patients receiving concomitant verapamil. May potentiate vecuronium-induced neuromuscular block.

**Avoid** unnecessary exposure of medication to sunlight. **Avoid** extravasation into tissues. A decrease in spasticity sufficient to allow daily function should be the therapeutic goal. Discontinue if benefits are not evident in 45 days.

**DAPSONE**

Aczone, Diaminodiphenylsulfone, DDS, and generics

**Antibiotic, sulfone derivative**

No



Yes



2



C

**Tabs:** 25, 100 mg**Oral suspension:** 2 mg/mL **Topical gel (Aczone):** 5% (30, 60, 90 g)**Pneumocystis jirovecii (formerly carinii) treatment:****Child and adult:** 2 mg/kg/24 hr PO once daily; **max. dose:** 100 mg/24 hr with trimethoprim 15 mg/kg/24 hr PO ÷ TID**Pneumocystis jirovecii (formerly carinii) prophylaxis (first episode and recurrence):****Child ≥ 1 mo:** 2 mg/kg/24 hr PO once daily; **max. dose** 100 mg/24 hr. Alternative weekly dosing, 4 mg/kg/dose PO Q7 days; **max. dose** 200 mg/dose.**Adult:** 100 mg/24 hr PO ÷ once daily–BID with or without pyrimethamine 50 mg PO Q7 days and leucovorin 25 mg PO Q7 days; other combination regimens with pyrimethamine and leucovorin may be used (see <http://www.hivatis.org>).**Toxoplasma gondii prophylaxis (prevent first episode):****Child ≥ 1 mo:** 2 mg/kg/24 hr (**max. dose:** 25 mg/24 hr) PO once daily with pyrimethamine 1 mg/kg/24 hr (max. 25 mg/dose) PO once daily and leucovorin 5 mg PO Q3 days.**Adult:** 50 mg PO once daily with pyrimethamine 50 mg PO Q7 days and leucovorin 25 mg PO Q7 days; other combination regimens with pyrimethamine and leucovorin may be used (see <http://www.hivatis.org>).**Leprosy (see [www.who.int/lep/disease/disease.htm](http://www.who.int/lep/disease/disease.htm) for latest recommendations, including combination regimens such as rifampin ± clofazimine):****Child:** 1–2 mg/kg/24 hr PO once daily; **max. dose** 100 mg/24 hr**Adult:** 50–100 mg PO once daily**Acne vulgaris (topical gel [Aczone]):**

≥ 12 yr: Apply small amount of topical gel onto clean, acne-affected areas BID.

Patients with HIV, glutathione deficiency, or G6PD deficiency may be at increased risk for developing methemoglobinemia. Side effects include hemolytic anemia (dose related), agranulocytosis, methemoglobinemia, aplastic anemia, nausea, vomiting, hyperbilirubinemia, headache, nephrotic syndrome, and hypersensitivity reaction (sulfone syndrome). Cholestatic jaundice, peripheral neuropathy, and suicidal intent have been reported with systemic use. Didanosine, rifabutin, and rifampin decrease dapsone levels. Trimethoprim increases dapsone levels. Pyrimethamine, nitrofurantoin, primaquine, and zidovudine increase risk for hematologic side effects.

Oral suspension may not be absorbed as well as tablets.

**TOPICAL USE:** Dry skin, erythema, and peeling of skin may occur. Use of topical gel, followed by benzoyl peroxide for acne, has resulted in temporary local discoloration (yellow/orange) of skin and facial hair.**DARBEPOETIN ALFA**

Aranesp

**Erythropoiesis stimulating protein**

Yes



No



?



C

**Injection:** 25, 40, 60, 100, 200, 300 mcg/1 mL (1 mL), 150 mcg/0.75 mL (0.75 mL)**Single-dose prefilled injection syringe (27-gauge ½-inch needle):** 25 mcg/0.42 mL, 40 mcg/0.4 mL, 60 mcg/0.3 mL, 100 mcg/0.5 mL, 150 mcg/0.3 mL, 200 mcg/0.4 mL, 300 mcg/0.6 mL, 500 mcg/1 mL. Both dosage forms contain polysorbate (0.05 mg/mL)

DARBEPOETIN ALFA *continued***Anemia in chronic renal failure (see remarks):****Child (>1 yr) and adult:**

**Receiving dialysis:** Start with 0.45 mcg/kg/dose IV/SC once weekly, **OR** 0.75 mcg/kg/dose IV/SC once Q2 wk; IV route is recommended for patients on hemodialysis. Adjust dose according to table that follows.

**Not receiving dialysis:** Start with 0.45 mcg/kg/dose IV/SC once Q4 wk, and adjust dose according to table that follows:

**Darbepoetin Alfa Dose Adjustment in Anemia Associated with Chronic Renal Failure**

Response to Dose	Dose Adjustment
<1 g/dL increase in hemoglobin and below target range after 4 wk of therapy	Increase dose by 25% not more frequently than once monthly. Further increases, if needed, may be done at 4-wk intervals.
>1 g/dL increase in hemoglobin in any 2-wk period, or if hemoglobin exceeds and approaches 11 g/dL	Decrease dose by 25%.
Hemoglobin continues to increase despite dosage reduction.	Discontinue therapy; reinstitute therapy at a 25% lower dose of the previous dose after hemoglobin starts to decrease.

**Anemia associated with chemotherapy (patients with nonmyeloid malignancies):**

**Child (limited data) and adult (see remarks):** Start with 2.25 mcg/kg/dose SC once weekly, and adjust dose according to table that follows:

**Darbepoetin Alfa Dose Adjustment in Anemia Associated with Chemotherapy**

Response to Dose	Dose Adjustment
<1 g/dL increase in hemoglobin and remains below 10 g/dL after 6 wk of therapy	Increase dose to 4.5 mcg/kg/dose once weekly SC/IV.
>1 g/dL increase in hemoglobin in any 2-wk period or when hemoglobin reaches a level needed to avoid transfusion	Decrease dose by 40%.
If hemoglobin exceeds a level needed to avoid transfusion	Hold therapy until hemoglobin approaches a level where transfusions may be required and restart at a reduced dose by 40%.
Lack of response after 8 wk or completion of chemotherapy	Discontinue therapy.

**Conversion from Epoetin Alfa to Darbepoetin Alfa (see table below):**

Previous Weekly Epoetin Alfa Dose (units/wk) <sup>1</sup>	PEDIATRIC Weekly Darbepoetin Alfa Dose (mcg/wk) Administered SC/IV Once Weekly <sup>2</sup>	ADULT Weekly Darbepoetin Alfa Dose (mcg/wk) Administered SC/IV Once Weekly <sup>2</sup>	ADULT Once Q2 wk Darbepoetin Alfa Dose (mcg Q2 wk) Administered SC/IV Once Q2 wk <sup>3</sup>
<1500	Insufficient data	6.25	12.5
1500–2499	6.25	6.25	12.5
2500–4999	10	12.5	25
5000–10,999	20	25	50
11,000–17,999	40	40	80
18,000–33,999	60	60	120
34,000–89,000	100	100	200
≥90,000	200	200	400

1. 200 units of epoetin alfa is equivalent to 1 mcg darbepoetin alfa.

2. If patient was receiving epoetin alfa 2–3 times weekly, darbepoetin alfa should be administered once weekly.

3. If patient was receiving epoetin alfa once weekly, darbepoetin alfa should be administered once Q2 wk.

DARBEPOETIN ALFA *continued*

**Contraindicated** in uncontrolled hypertension and patients hypersensitive to albumin/polysorbate 80 or epoetin alfa. Darbepoetin alfa is not intended for patients requiring acute correction of anemia. **Use with caution** in seizures and liver disease. Evaluate serum iron, ferritin, and TIBC; concurrent iron supplementation may be necessary. Red cell aplasia and severe anemia associated with neutralizing antibodies to erythropoietin have been reported.



**USE IN CHRONIC RENAL FAILURE:** In pediatric patients, higher doses may be needed for individuals being switched from epoetin alfa compared with naïve patients. May cause edema, fatigue, GI disturbances, headache, blood pressure changes, fever, cardiac arrhythmia/arrest, infections, and myalgia. Higher risk for mortality and serious cardiovascular events have been reported with higher targeted hemoglobin levels (>11 g/dL). If hemoglobin levels do not increase or reach targeted levels despite appropriate dose titrations over a 12-wk period, (1) **do not** administer higher doses, and use the lowest dose that will maintain hemoglobin levels to avoid the need for recurrent blood transfusions; (2) evaluate and treat other causes of anemia; (3) always follow the dose adjustment instructions; and (4) discontinue use if patient remains transfusion dependent.

**USE IN CANCER:** Use only for anemia due to myelosuppressive chemotherapy; not effective in reducing the need for transfusions in patients with anemia not due to chemotherapy. Shortened survival and time to tumor progression have been reported in patients with various cancers. May cause fatigue, fever, edema, dizziness, headache, GI disturbances, arthralgia/myalgia, and rash. Use lowest dose to avoid transfusions and **do not** exceed hemoglobin levels >12 g/dL; increased frequency of adverse events, including mortality and thrombotic vascular events, have been reported. **Prescribers and hospitals must enroll in and comply with the ESA APPRISE Oncology Program to prescribe and/or dispense this drug to cancer patients.**

Monitor hemoglobin, BP, serum chemistries, and reticulocyte count. Increases in dose should not be made more frequently than once a month. For IV administration, infuse over 1–3 min.

**DEFEROXAMINE MESYLATE**

Desferal and generics

**Chelating agent**

Yes



Yes



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C

Injection: 500, 2000 mg

**Acute iron poisoning (if using IV route, convert to IM as soon as patient's clinical condition permits [see remarks]):**

**Child:****IV:** 15 mg/kg/hr**IM:** 50 mg/kg/dose Q6 hr**Max. dose:** 6 g/24 hr**Adult:****IV:** 15 mg/kg/hr**IM:** 1 g × 1, then 0.5 g Q4 hr × 2; may repeat 0.5 g Q4–12 hr**Max. dose:** 6 g/24 hr

**Chronic iron overload (see remarks):**

**Child and adolescent:**

**IV:** 20–40 mg/kg/dose over 8–12 hr once daily × 5–7 days per week; usual **max. doses** are 40 mg/kg/24 hr (child) or 60 mg/kg/24 hr (adolescent)

**SC:** 20–40 mg/kg/dose once daily as infusion over 8–12 hr; **max. dose** 2 g/24 hr

DEFEROXAMINE MESYLATE *continued***Adult:**

**IV:** 40–50 mg/kg/dose over 8–12 hr once daily  $\times$  5–7 days per week; **max. dose** 6 g/24 hr

**IM:** 0.5–1 g/dose once daily

**SC:** 1–2 g/dose once daily as infusion over 8–24 hr



**Contraindicated** in severe renal disease or anuria. **Not approved** for use in primary hemochromatosis. May cause flushing, erythema, urticaria, hypotension, tachycardia, diarrhea, leg cramps, fever, cataracts, hearing loss, nausea, and vomiting. Iron mobilization may be poor in children <3 yr. Serum creatinine elevation, acute renal failure, renal tubular disorders, and hepatic dysfunction have been reported.

**Avoid** use if GFR < 10 mL/min, and administer 25%–50% of usual dose if GFR is 10–50 mL/min or patient is receiving continuous renal replacement therapy (CRRT).

High doses and concomitant low ferritin levels have also been associated with growth retardation.

Growth velocity may resume to pretreatment levels by reducing the dosage. Acute respiratory distress syndrome has been reported after treatment with excessively high IV doses in patients with acute iron intoxication or thalassemia. Toxicity risk has been reported with infusions >8 mg/kg/hr for >4 days for thalassemia, and with infusions of 15 mg/kg/hr for >1 day for acute iron toxicity. Pulmonary toxicity was not seen in 193 courses.

For IV infusion, **maximum rate:** 15 mg/kg/hr. Infuse IV infusion over 6–12 hr for mild/moderate iron intoxication and over 24 hr for severe cases, then reassess. SC route is via a portable controlled infusion device and is **not recommended** in acute iron poisoning.

**DESMOPRESSIN ACETATE**

DDAVP, Stimate, and generics

**Vasopressin analog, synthetic; hemostatic agent**



No



No



2



B

**Tabs:** 0.1, 0.2 mg

**Nasal solution (with rhinal tube):** DDAVP, 100 mcg/mL (2.5 mL); contains 9 mg NaCl/mL

**Injection:** 4 mcg/mL (1, 10 mL); contains 9 mg NaCl/mL

**Nasal spray:**

100 mcg/mL, 10 mcg/spray (50 sprays, 5 mL); contains 7.5 mg NaCl/mL

Stimate: 1500 mcg/mL, 150 mcg/spray (25 sprays, 2.5 mL); contains 9 mg NaCl/mL

**Conversion:** 100 mcg = 400 IU arginine vasopressin

**Diabetes insipidus (see remarks):****Oral:**

**Child  $\leq$  12 yr:** Start with 0.05 mg/dose BID; titrate to effect; usual dose range: 0.1–0.8 mg/24 hr.

**Child > 12 yr and adult:** Start with 0.05 mg/dose BID; titrate dose to effect; usual dose range: 0.1–1.2 mg/24 hr  $\div$  BID–TID.

**Intranasal (titrate dose to achieve control of excessive thirst and urination. Morning and evening doses should be adjusted separately for diurnal rhythm of water turnover):**

**3 mo–12 yr:** 5–30 mcg/24 hr  $\div$  once daily–BID

**> 12 yr and adult:** 10–40 mcg/24 hr  $\div$  once daily–TID

**IV/SC:**

**< 12 yr (limited data):** 0.1–1 mcg/24 hr  $\div$  once daily–BID; start with lower dose and increase as needed.

**$\geq$  12 yr and adult:** 2–4 mcg/24 hr  $\div$  BID

*Continued*



DESMOPRESSIN ACETATE *continued***Hemophilia A and von Willebrand disease:****Intranasal:** 2–4 mcg/kg/dose 2 hr before procedure**IV:** 0.2–0.4 mcg/kg/dose over 15–30 min, administered 30 min before procedure**Nocturnal enuresis ( $\geq 6$  yr [see remarks]):****Oral:** 0.2 mg at bedtime, titrated to a **max. dose** of 0.6 mg to achieve desired effect

**Use with caution** in hypertension, patients at risk for water intoxication with hyponatremia, and coronary artery disease. May cause headache, nausea, seizures, blood pressure changes, hyponatremia, nasal congestion, abdominal cramps, and hypertension.

**NOCTURNAL ENURESIS:** Intranasal formulations are no longer indicated by the FDA for primary nocturnal enuresis (children are susceptible for severe hyponatremia and seizures) or in patients with a history of hyponatremia. Patients using tablets should reduce their fluid intake to prevent potential water intoxication and hyponatremia, and have their therapy interrupted during acute illnesses that may lead to fluid and/or electrolyte imbalance.

Injection may be used SC or IV at  $\approx 10\%$  of intranasal dose. Adjust fluid intake to decrease risk of water intoxication, and monitor serum sodium.

If switching stabilized patient from intranasal route to IV/SC route, use 10% of intranasal dose. Peak effects: 1–5 hr with intranasal route, 1.5–3 hr with IV route, and 2–7 hr with PO route.

**DEXAMETHASONE**

Decadron, Dexpak Taperpak, Hexadrol, Maxidex, and many generics

**Corticosteroid**

No



No



3



C

**Tabs (Decadron and generics):** 0.5, 0.75, 1, 1.5, 2, 4, 6 mg**Dexpak Taperpak:** 1.5 mg (21 tabs [6 day], 35 tabs [10 day], 51 tabs [13 day])**Injection (sodium phosphate salt):** 4, 10 mg/mL (some preparations contain benzyl alcohol or methyl/propyl parabens)**Elixir:** 0.5 mg/5 mL (some preparations contain 5% alcohol)**Oral solution:** 0.1, 1 mg/mL (some preparations contain 30% alcohol)**Ophthalmic solution:** 0.1% (5 mL)**Ophthalmic suspension (Maxidex):** 0.1% (5 mL)

**Airway edema:** 0.5–2 mg/kg/24 hr IV/IM  $\div$  Q6 hr (begin 24 hr before extubation, and continue for 4–6 doses after extubation)

**Croup:** 0.6 mg/kg/dose PO/IV/IM  $\times$  1

**Antiemetic (chemotherapy induced):****Initial:** 10 mg/m<sup>2</sup>/dose IV; **max. dose** 20 mg**Subsequent:** 5 mg/m<sup>2</sup>/dose Q6 hr IV**Anti-inflammatory:****Child:** 0.08–0.3 mg/kg/24 hr PO, IV, IM  $\div$  Q6–12 hr**Adult:** 0.75–9 mg/24 hr PO, IV, IM  $\div$  Q6–12 hr**Brain tumor–associated cerebral edema:****Loading dose:** 1–2 mg/kg/dose IV/IM  $\times$  1**Maintenance:** 1–1.5 mg/kg/24 hr  $\div$  Q4–6 hr; **max. dose** 16 mg/24 hr**Ophthalmic use (child and adult):**

**Ointment:** Apply a thin coating of ointment to conjunctival sac of affected eye(s) TID–QID. When a favorable response is achieved, reduce daily dosage to BID and later to once daily as a maintenance dose sufficient to control symptoms.

DEXAMETHASONE *continued*

**Solution:** Instill 1 to 2 drops into conjunctival sac of affected eye(s) Q1 hr during the day and Q2 hr during the night as initial therapy. When a favorable response is achieved, reduce dosage to 1 drop Q4 hr. Further dose reduction to 1 drop TID–QID may be sufficient to control symptoms.

**Suspension:** Shake well before using. Instill 1–2 drops into conjunctival sacs of affected eye(s). For severe disease, drops may be used Q1 hr, then tapered to discontinuation as inflammation subsides. For mild disease, drops may be used  $\leq 4$ –6 times/24 hr.

**Not recommended** for systemic therapy in prevention or treatment of chronic lung disease in infants with very low birth weight, owing to increased risk for adverse events (*Pediatrics*. 2002;109:330–338). Dexamethasone is a substrate of CYP P450 3A3/4 and P-glycoprotein.



**Toxicity:** Same as for prednisone without mineralocorticoid effects. **Contraindicated** in active untreated infections and fungal, viral, and mycobacterial ocular infections.

**OPHTHALMIC USE:** Use ophthalmic preparation only in consultation with an ophthalmologist. **Use with caution** in corneal/scleral thinning and glaucoma. Consider the possibility of persistent fungal infections of the cornea after prolonged use. Ophthalmic solution/suspension may be used in otitis externa.

Oral peak serum levels occur 1–2 hr and within 8 hr after IM administration. **For other uses, doses based on body surface area and dose equivalence to other steroids; see Chapters 10 and 30.**

## DEXMEDETOMIDINE

Precedex

**$\alpha$ -Adrenergic agonist, sedative**



Yes



No



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C

**Injection:** 200 mcg/2 mL (2 mL); preservative free

**Premixed injection:** 200 mcg/50 mL (50 mL), 400 mcg/100 mL (100 mL); preservative free

**NOTE:** Maintenance infusion rate dosing metric is mcg/kg/hr.

**ICU sedation:**

**Child (limited data):** 0.5–2 mcg/kg/dose IV  $\times$  1 over 10 min, followed by 0.2–1 mcg/kg/hr infusion titrated to effect. Children <1 yr of age may require higher dosages.

**Adult:** 1 mcg/kg/dose IV  $\times$  1 over 10 min, followed by 0.2–0.7 mcg/kg/hr infusion and titrated to effect.

**Procedural sedation:****Child (limited data):**

**IV:** 2 mcg/kg/dose  $\times$  1 IV, followed by 1.5 mcg/kg/hr was administered to children with autism/pervasive developmental disorders for sedation for EEG.

**IM:** 1–4.5 mcg/kg/dose  $\times$  1 IM was administered to children for sedation for EEG. Extremely anxious, inconsolable, aggressive, and noncompliant children received doses  $>2.5$  mcg/kg; calm and relatively compliant children received doses  $\leq 2.5$  mcg/kg. A second lower repeat dose ( $\approx 2$  mcg/kg/dose IM) was administered if adequate sedation was not achieved after 10 min after the first dose.

**Intranasal route (limited data):** 1–2 mcg/kg/dose  $\times$  1 for premedication anesthesia induction.

**Adult:** 1 mcg/kg/dose IV  $\times$  1 over 10 min, followed by 0.6 mcg/kg/hr titrated to effect; dosage has ranged from 0.2–1 mcg/kg/hr.

*Continued*

DEXMEDETOMIDINE *continued*

**Use with caution** with other vasodilating or negative chronotropic agents (additive pharmacodynamic effects), hepatic impairment (decrease drug clearance; consider dose reduction), advanced heart block, hypovolemia, diabetes mellitus, chronic hypertension, and severe ventricular dysfunction. Prolonged use >24 hr may be associated with tolerance and tachyphylaxis and dose-related side effects (ARDS, respiratory failure, agitation).

Hypotension, bradycardia, and dry mouth are common side effects. Transient hypertension has been observed during loading doses. **Do not** abruptly withdraw therapy; withdrawal symptoms (nausea, vomiting, agitation) are possible. Taper dose when discontinuing use.

Use with anesthetics, sedatives, hypnotics, and opioids may lead to enhanced effects; consider dosage reduction of dexmedetomidine. Dexmedetomidine is a CYP 450 2A6 substrate and a weak inhibitor of CYP 450 1A2, 2C9, and 3A4.

Onset of action for procedural sedation: IV or IM, 15 min; intranasal, 15–30 min. Duration of action for procedural sedation: IM, 1 hr; intranasal, 1–1.5 hr.

Use of this drug should be administered by individuals skilled in the management of patients in the ICU and OR. Concentrated IV solution must be diluted with NS to a concentration of 4 mcg/mL before administration. See Chapter 6 for additional information.

**DEXMETHYLPHENIDATE**

Focalin, Focalin XR, and generics

**CNS stimulant**



No



No



3



C

**Tab (Focalin and generics):** 2.5, 5, 10 mg

**Extended-release caps (Focalin XR):** 5, 10, 15, 20, 25, 30, 35, 40 mg

**Attention deficit/hyperactivity disorder:**

**METHYLPHENIDATE NAIVE:**



Age/Dosage Form	Initial Dose	Dosage Increase at Weekly Intervals (If Needed)	Daily Maximum Dose
<b>≥6 yr and adolescent</b>			
Immediate-release tabs*	2.5 mg PO BID	2.5–5 mg/24 hr	20 mg/24 hr (10 mg BID)
Extended-release caps†	5 mg PO once daily	5 mg/24 hr	30 mg/24 hr
<b>Adult</b>			
Immediate-release tabs*	2.5 mg PO BID	2.5–5 mg/24 hr	20 mg/24 hr (10 mg BID)
Extended-release caps†	10 mg PO once daily	10 mg/24 hr	40 mg/24 hr

\*BID dosing.

†Once-daily dosing.

**CONVERTING FROM METHYLPHENIDATE:**

**≥6 yr and adult:** Start at 50% of the total daily dose of racemic methylphenidate with the following maximum doses:

**Immediate-release tabs (BID dosing):** 20 mg/24 hr

**Extended-release caps (once-daily dosing):** 30 mg/24 hr for ≥6 yr–adolescents; 40 mg/24 hr for adults

DEXMETHYLPHENIDATE *continued***CONVERTING FROM IMMEDIATE-RELEASE TABS (BID) TO EXTENDED-RELEASE CAPS (once daily)****DEXMETHYLPHENIDATE:** Use the equivalent mg dosage amount.

Dexmethylphenidate is the *D*-enantiomer of methylphenidate and accounts for the majority of clinical effects for methylphenidate. **Contraindicated** in glaucoma, anxiety disorders, motor tics, and Tourette syndrome. **Do not** use with MAO inhibitors; hypertensive crisis may occur if used within 14 days of discontinuance of MAO inhibitor. See *Methylphenidate* for additional warnings and drug interactions.

Common side effects include abdominal pain, indigestion, appetite suppression, nausea, headache, insomnia, and anxiety.

Immediate-release tablets are dosed BID (minimum 4 hr between doses), and extended-release capsules are dosed once daily. Contents of the extended-release capsule may be sprinkled on a spoonful of applesauce and consumed immediately for those who are unable to swallow capsules.

**DEXTROAMPHETAMINE ± AMPHETAMINE**

Dexedrine, ProCentra, Zenzedi, and many generics

In combination with amphetamine: Adderall, Adderall XR, and generics

**CNS stimulant, amphetamine**



No



No



X



C

**Tab (Zenzedi and generics):** 2.5, 5, 7.5, 10 mg


**Sustained-release caps (Dexedrine and generics):** 5, 10, 15 mg

**Oral solution (ProCentra and generics):** 1 mg/mL (473 mL)

**In combination with amphetamine (Adderall):** Available as 1:1:1:1 mixture of dextroamphetamine sulfate, dextroamphetamine saccharate, amphetamine aspartate, and amphetamine sulfate salts (e.g., 5 mg tablet contains 1.25 mg dextroamphetamine sulfate, 1.25 mg dextroamphetamine saccharate, 1.25 mg amphetamine aspartate, and 1.25 mg amphetamine sulfate):

**Tab:** 5, 7.5, 10, 12.5, 15, 20, 30 mg

**Caps, extended-release (Adderall XR and generics):** 5, 10, 15, 20, 25, 30 mg

**Oral suspension:** 1 mg/mL 

**Dosages are in terms of mg of dextroamphetamine when using dextroamphetamine alone**

**OR in terms of mg of the total dextroamphetamine and amphetamine salts when using Adderall. Non-extended-release dosage forms are usually given BID–TID (first dose on awakening and subsequent doses at intervals of 4–6 hr later). Extended/sustained-released dosage forms are usually given PO once daily, sometimes BID.**

**Attention deficit/hyperactivity disorder:**

**3–5 yr:** 2.5 mg/24 hr QAM; increase by 2.5 mg/24 hr at weekly intervals to a **max. dose** of 40 mg/24 hr ÷ once daily–TID.

**≥ 6 yr:** 5 mg/24 hr QAM; increase by 5 mg/24 hr at weekly intervals to a **max. dose** of 40 mg/24 hr ÷ once daily–TID.

**Narcolepsy:**

**6–12 yr:** 5 mg/24 hr ÷ once daily–TID; increase by 5 mg/24 hr at weekly intervals to a **max. dose** of 60 mg/24 hr

**> 12 yr and adult:** 10 mg/24 hr ÷ once daily–TID; increase by 10 mg/24 hr at weekly intervals to a **max. dose** of 60 mg/24 hr

**Use with caution** in presence of hypertension or cardiovascular disease. **Avoid** use in known serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious cardiac problems that may increase



*Continued*

DEXTROAMPHETAMINE ± AMPHETAMINE *continued*

risk of sympathomimetic effects of amphetamines (sudden death, stroke, and MI have been reported). **Do not** give with MAO inhibitors or general anesthetics.

**Not recommended** for patients <age 3 yr. Medication should generally **not** be used in children <5 yr, because diagnosis of ADHD in this age group is extremely difficult (use in consultation with a specialist). Interrupt administration occasionally to determine need for continued therapy. Many side effects, including insomnia (**avoid** dose administration within 6 hr of bedtime), restlessness, anorexia, psychosis, visual disturbances, headache, vomiting, abdominal cramps, dry mouth, and growth failure. Paranoia, mania, peripheral vasculopathy (including Raynaud phenomenon), and auditory hallucination have been reported. Tolerance develops. Same guidelines as for methylphenidate apply.

**DIAZEPAM**

Valium, Diastat, Diastat AcuDial, and various generics

**Benzodiazepine; anxiolytic, anticonvulsant**



Yes



Yes



X



D

**Tabs:** 2, 5, 10 mg

**Oral solution:** 1 mg/mL, 5 mg/mL (contains 19% alcohol)

**Injection:** 5 mg/mL (contains 40% propylene glycol, 10% alcohol, 5% sodium benzoate, and 1.5% benzyl alcohol)

**Rectal gel:**

**Pediatric rectal gel (Diastat and generics):** 2.5 mg (5 mg/mL concentration with 4.4-cm rectal tip delivery system; contains 10% alcohol, 1.5% benzyl alcohol, and propylene glycol); in twin packs

**Pediatric/Adult rectal gel (Diastat AcuDial and generics):**

**4.4-cm rectal tip delivery system (Pediatric/Adult):** 10 mg (5 mg/mL delivers set doses of either 5, 7.5, or 10 mg); contains 10% alcohol and 1.5% benzyl alcohol; in twin packs

**6-cm rectal tip delivery system (Adult):** 20 mg (5 mg/mL delivers set doses of either 10, 12.5, 15, 17.5, 20 mg); contains 10% alcohol and 1.5% benzyl alcohol; in twin packs

**Sedative/muscle relaxant:**

**Child:**

**IM or IV:** 0.04–0.2 mg/kg/dose Q2–4 hr; **max. dose** 0.6 mg/kg within an 8-hr period

**PO:** 0.12–0.8 mg/kg/24 hr ÷ Q6–8 hr

**Adult:**

**IM or IV:** 2–10 mg/dose Q3–4 hr PRN

**PO:** 2–10 mg/dose Q6–12 hr PRN

**Status epilepticus:**

**Neonate:** 0.3–0.75 mg/kg/dose IV Q15–30 min × 2–3 doses; **max. total dose:** 2 mg.

**Child > 1 mo:** 0.2–0.5 mg/kg/dose IV Q15–30 min; **max. total dose** <5 yr, 5 mg; ≥5 yr, 10 mg. May repeat dosing in 2–4 hr as needed.

**Adult:** 5–10 mg/dose IV Q10–15 min; **max. total dose** 30 mg in an 8-hr period. May repeat dosing in 2–4 hr as needed.

**Rectal dose (using IV dosage form):** 0.5 mg/kg/dose, followed by 0.25 mg/kg/dose in 10 min PRN.

**Rectal gel:** All doses rounded to nearest available dosage strength; repeat dose in 4–12 hr PRN.

**2–5 yr:** 0.5 mg/kg/dose

**6–11 yr:** 0.3 mg/kg/dose

**≥12 yr and adult:** 0.2 mg/kg/dose

**Contraindicated** in myasthenia gravis, severe respiratory insufficiency, severe hepatic failure, and sleep apnea syndrome. Hypotension and respiratory depression may occur. **Use with caution** in hepatic and renal dysfunction, glaucoma, shock, and depression. **Do not** use in combination with protease inhibitors. Concurrent use with CNS depressants, cimetidine, erythromycin, itraconazole, and valproic acid may enhance effects of diazepam. Diazepam is



DIAZEPAM *continued*

a substrate for CYP P450 2B6, 2C8, 2C9, and 3A5–7 and a minor substrate and inhibitor for CYP P450 2C19 and 3A3/4. The active desmethyldiazepam metabolite is a CYP P450 2C19 substrate.

Administer the conventional IV product undiluted no faster than 2 mg/min. **Do not** mix with IV fluids. In status epilepticus, diazepam must be followed by long-acting anticonvulsants. Onset of anticonvulsant effect: 1–3 min with IV route, 2–10 min with rectal route. **For management of status epilepticus, see Chapter 1.**

**DIAZOXIDE**

Proglycem

**Antihypoglycemic agent, antihypertensive agent**



No



Yes



?



C

**Oral suspension:** 50 mg/mL (30 mL); contains 7.25% alcohol

**Hyperinsulinemic hypoglycemia (due to insulin-producing tumors; start at the lowest dose):**

**Newborn and infant:** 8–15 mg/kg/24 hr ÷ Q8–12 hr PO;

usual range: 5–20 mg/kg/24 hr ÷ Q8 hr

**Child and adult:** 3–8 mg/kg/24 hr ÷ Q8–12 hr PO



Hypoglycemia should be treated initially with IV glucose; diazoxide should be introduced only if refractory to glucose infusion. Should **not** be used in patients hypersensitive to thiazides unless benefit outweighs risk. **Use with caution** in renal impairment (clearance of drug is reduced); consider dosage reduction.



Sodium and fluid retention is common in young infants and adults and may precipitate CHF in patients with compromised cardiac reserve (usually responsive to diuretics). Hirsutism (reversible), GI disturbances, transient loss of taste, tachycardia, ketoacidosis, palpitations, rash, headache, weakness, and hyperuricemia may occur. Monitor BP closely for hypotension.

Hyperglycemic effect with PO administration occurs within 1 hr, with a duration of 8 hr.

**DICLOXACILLIN SODIUM**

Dycill, Pathocil, and generics

**Antibiotic, penicillin (penicillinase-resistant)**



No



No



1



B

**Caps:** 250, 500 mg; contains 0.6 mEq Na/250 mg

**Child (<40 kg) (see remarks):**

**Mild/moderate infections:** 12.5–50 mg/kg/24 hr PO ÷ Q6 hr

**Severe infections:** 50–100 mg/kg/24 hr PO ÷ Q6 hr

**Max. dose:** 2 g/24 hr

**Child (≥40 kg) and adult:** 125–500 mg/dose PO Q6 hr; **max. dose** 2 g/24 hr



**Contraindicated** in patients with a history of penicillin allergy. **Use with caution** in cephalosporin hypersensitivity. May cause nausea, vomiting, and diarrhea. Immune hypersensitivity has been reported.



Limited experience in neonates and very young infants. Higher doses (50–100 mg/kg/24 hr) are indicated after IV therapy for osteomyelitis.

May decrease effects of oral contraceptives and warfarin. Administer 1 hr before meals or 2 hr after meals.

**DIGOXIN**

Lanoxin, Lanoxin Pediatric, and generics

**Antiarrhythmic agent, inotrope**

No



Yes



2



C

**Tab:** 125, 250 mcg**Oral solution:** 50 mcg/mL (60 mL); may contain 10% alcohol**Injection:**

Lanoxin Pediatric: 100 mcg/mL (1 mL); may contain propylene glycol and alcohol

Lanoxin and generics: 250 mcg/mL (1, 2 mL); may contain propylene glycol and alcohol

**Digitalizing:** Total digitalizing dose (TDD) and maintenance doses in mcg/kg/24 hr (see table that follows):**DIGOXIN DIGITALIZING AND MAINTENANCE DOSES**

Age	TDD		Daily Maintenance	
	PO	IV/IM	PO	IV/IM
Premature neonate	20	15	5	3–4
Full-term neonate	30	20	8–10	6–8
1 mo–<2 yr	40–50	30–40	10–12	7.5–9
2–10 yr	30–40	20–30	8–10	6–8
>10 yr and < 100 kg	10–15	8–12	2.5–5	2–3

**Initial:** ½ TDD, then ¼ TDD Q8–18 hr × 2 doses; obtain ECG 6 hr after dose to assess for toxicity.**Maintenance:**

&lt;10 yr: Give maintenance dose ÷ BID.

≥10 yr: Give maintenance dose once daily.

**Contraindicated** in patients with ventricular dysrhythmias. Use should be **avoided** in patients with preserved left ventricular systolic function. **Use with caution** in renal failure, with calcium channel blockers (may result in heart block), and with adenosine (enhanced depressant effects on SA and AV nodes). May cause AV block or dysrhythmias. In patients treated with digoxin, cardioversion or calcium infusion may lead to ventricular fibrillation (pretreatment with lidocaine may prevent this). Patients with beri-beri heart disease may not respond to digoxin if underlying thiamine deficiency is not treated concomitantly. Decreased serum potassium and magnesium, or increased magnesium and calcium, may increase risk for digoxin toxicity. For signs and symptoms of toxicity, see Chapter 2.



Excreted via kidney; **adjust dose in renal failure (see Chapter 31)**. Therapeutic concentration: 0.8–2 ng/mL. Higher doses may be required for supraventricular tachycardia. Neonates, pregnant women, and patients with renal, hepatic, or heart failure may have falsely elevated digoxin levels due to the presence of digoxin-like substances.

Digoxin is a CYP 450 3A4 and P-glycoprotein substrate. Calcium channel blockers, carvedilol, amiodarone, quinidine, cyclosporine, itraconazole, and macrolide antibiotics may increase digoxin levels. Use with β-blockers may increase risk for bradycardia. Succinylcholine may cause arrhythmias in digitalized patients.

**T<sub>1/2</sub>:** Premature infants, 61–170 hr; full-term neonates, 35–45 hr; infants, 18–25 hr; and children, 35 hr.

Recommended serum sampling at steady state: Obtain a single level from 6 hr post dose to just before next scheduled dose after 5–8 days of continuous dosing. Levels obtained before steady state may be useful in preventing toxicity.

**DIGOXIN IMMUNE FAB (OVINE)**

DigiFab

*Antidigoxin antibody*

No



Yes



?



C

Injection: 40 mg

**Dosing based on known amounts of digoxin acutely ingested:****First determine total body digoxin load (TBL):**TBL (mg) = mg digoxin ingested  $\times$  0.8**Then, calculate digoxin immune Fab dose:**Dose in number of digoxin immune Fab vials (DigiFab): # vials = TBL  $\div$  0.5

Dosing based on steady-state serum digoxin levels:

**DIGIFAB DOSE (MG) FROM STEADY-STATE DIGOXIN LEVELS**

Patient Weight (kg)	Serum Digoxin Concentration (ng/mL)						
	1	2	4	8	12	16	20
1	0.4 mg*	1 mg*	1.5 mg*	3 mg*	5 mg	6.5 mg	8 mg
3	1 mg*	2.5 mg*	5 mg	10 mg	14 mg	19 mg	24 mg
5	2 mg*	4 mg	8 mg	16 mg	24 mg	32 mg	40 mg
10	4 mg	8 mg	16 mg	32 mg	48 mg	64 mg	80 mg
20	8 mg	16 mg	32 mg	64 mg	96 mg	128 mg	160 mg
40	20 mg	40 mg	80 mg	120 mg	200 mg	280 mg	320 mg
60	20 mg	40 mg	120 mg	200 mg	280 mg	400 mg	480 mg
70	40 mg	80 mg	120 mg	240 mg	360 mg	440 mg	560 mg
80	40 mg	80 mg	120 mg	280 mg	400 mg	520 mg	640 mg
100	40 mg	80 mg	160 mg	320 mg	480 mg	640 mg	800 mg

\*Use 1 mg/mL DigiFab concentration for dose accuracy.

**Dosage administration:**

Reconstitute each vial with 4 mL NS for a 10 mg/mL concentration and infuse IV dose over 30 min. If an infusion rate reaction occurs, stop infusion and restart at a slower rate. In situations of cardiac arrest, DigiFab can be administered as a bolus injection, but expect an increased risk for infusion-related reactions. For smaller doses, vials may be reconstituted with 36 mL NS for a 1 mg/mL concentration.

**Contraindicated** if hypersensitive to sheep products. **Use with caution** in renal or cardiac failure. May cause rapidly developing severe hypokalemia, decreased cardiac output (due to withdrawal of digoxin's inotropic effects), rash, edema and phlebitis. Digoxin therapy may be reinstituted in 3–7 days when toxicity has been corrected. Digoxin immune FAB will interfere with digitalis immunoassay measurements, resulting in misleading concentrations.

**DILTIAZEM**

Cardizem, Cardizem SR, Cardizem CD, Cardizem LA, Matzim LA, Dilacor XR, Tiazac, and many others, including generics

**Calcium channel blocker, antihypertensive**

Yes



Yes



1



C

**Tabs:** 30, 60, 90, 120 mg**Extended-release tabs:**

Cardizem LA: 120, 180, 240, 300, 360, 420 mg

Matzim LA: 180, 240, 300, 360, 420 mg

Continued




DILTIAZEM *continued***Extended-release caps:**

Various generics: 60, 90, 120, 180, 240, 300, 360, 420 mg

Cardizem CD: 120, 180, 240, 300, 360 mg

Dilacor XR: 120, 180, 240 mg

Tiazac: 120, 180, 240, 300, 360, 420 mg

**Oral liquid:** 12 mg/mL **Injection:** 5 mg/mL (5, 10, 25 mL)

**Child:** 1.5–2 mg/kg/24 hr PO ÷ TID–QID, **max. dose** 3.5 mg/kg/24 hr; **alternative max. doses** of 6 mg/kg/24 hr up to 360 mg/24 hr have been recommended.

**Adolescent and adult:****Immediate-release:** 30–120 mg/dose PO TID–QID; usual range 180–360 mg/24 hr**Extended-release:** 120–360 mg/24 hr PO ÷ once daily–BID (BID dosing with Cardizem SR; once-daily dosing with Cardizem CD, Cardizem LA, Matzim LA, Dilacor XR, Tiazac); **max. dose** 540 mg/24 hr

**Contraindicated** in acute MI with pulmonary congestion, second- or third-degree heart block, and sick sinus syndrome. **Use with caution** in CHF or renal and hepatic impairment.

Dizziness, headache, edema, nausea, vomiting, heart block, and arrhythmias may occur.

Monitor heart rate with concurrent clonidine use (sinus bradycardia has been reported).

Diltiazem is a substrate and inhibitor of the CYP 450 3A4 enzyme system. May increase levels and/or effect of buspirone, cyclosporine, carbamazepine, fentanyl, digoxin, quinidine, tacrolimus, benzodiazepines, and  $\beta$ -blockers. Cimetidine and statins may increase diltiazem serum levels.

Rifampin may decrease diltiazem serum levels.

Maximal antihypertensive effect seen within 2 wk.

**DIMENHYDRINATE**

Dramamine, other brand names, and generics

**Antiemetic, antihistamine**

No



No



3



B

**Tabs [OTC]:** 50 mg**Chewable tabs [OTC]:** 50 mg; contains 1.5 mg phenylalanine**Injection:** 50 mg/mL; contains benzyl alcohol and propylene glycol**Child (<12 yr):** 5 mg/kg/24 hr ÷ Q6 hr PO/IM/IV; alternative oral dosing by age:**2–5 yr:** 12.5–25 mg/dose Q6–8 hr PRN PO, with the **max. dosage** in the subsequent list**6–12 yr:** 25–50 mg/dose Q6–8 hr PRN PO, with the **max. dosage** in the subsequent list**≥12 yr and adult:** 50–100 mg/dose Q4–6 hr PRN PO/IM/IV**MAXIMUM PO DOSE:****2–5 yr:** 75 mg/24 hr**6–12 yr:** 150 mg/24 hr**≥12 yr and adult:** 400 mg/24 hr**MAXIMUM IM DOSE:****Child:** 300 mg/24 hr

Causes drowsiness and anticholinergic side effects. May mask vestibular symptoms and cause CNS excitation in young children. **Caution** when taken with ototoxic agents or history of seizures. **Use should be limited to management of prolonged vomiting of known etiology.**

**Not recommended** in children <2 yr. Toxicity resembles anticholinergic poisoning.

**DIMERCAPROL**

BAL, British Anti-Lewisite, and generics

**Heavy metal chelator (arsenic, gold, mercury, lead)**

Yes



Yes



?



C

**Injection (in oil):** 100 mg/mL; contains 20% benzyl benzoate and peanut oil (3 mL)**Give all injections deep IM.****Lead poisoning:****Acute severe encephalopathy (lead level > 70 mcg/dL):** 4 mg/kg/dose Q4 hr  $\times$  2–7 days, with the addition of Ca-EDTA (given at separate site) at the time of second dose.**Less severe poisoning:** 4 mg/kg  $\times$  1, then 3 mg/kg/dose Q4 hr  $\times$  2–7 days.**Arsenic or gold poisoning (see table below):**

	Mild Cases	Severe Cases
Days 1 and 2	2.5 mg/kg/dose Q6 hr	3 mg/kg/dose Q4 hr
Day 3	2.5 mg/kg/dose Q12 hr	3 mg/kg/dose Q6 hr
Days 4–13	2.5 mg/kg/dose Q24 hr	3 mg/kg/dose Q12 hr

**Mercury poisoning:** 5 mg/kg  $\times$  1, then 2.5 mg/kg/dose once daily–BID  $\times$  10 days**Contraindicated** in hepatic or renal insufficiency. May cause hypertension, tachycardia, GI disturbance, headache, fever (30% of children), nephrotoxicity, transient neutropenia. Symptoms are usually relieved by antihistamines. Urine should be kept alkaline to protect kidneys. **Use with caution** with G6PD deficiency and peanut-sensitive patients. **Do not** use concomitantly with iron.**DIPHENHYDRAMINE**

Benadryl and many other brand names and generics

**Antihistamine**

No



Yes



3



B

**Elixir (OTC):** 12.5 mg/5 mL; may contain 5.6% alcohol**Syrup (OTC):** 12.5 mg/5 mL; some may contain 5% alcohol**Oral liquid/solution (OTC):** 12.5 mg/5 mL**Caps/Tabs (OTC):** 25, 50 mg**Tabs, orally disintegrating (OTC):** 12.5 mg; contains aspartame, phenylalanine**Strips, orally disintegrating (OTC):** 12.5, 25 mg; may contain <5% alcohol**Chewable tabs (OTC):** 12.5 mg; contains aspartame, phenylalanine**Injection:** 50 mg/mL**Cream (OTC):** 1, 2% (30 g)**Topical gel (OTC):** 1% (37.5 g), 2% (120 g)**Topical spray (OTC):** 1.2% (60 mL)**Severe allergic reaction (anaphylaxis) and dystonic reactions (including phenothiazine toxicity) (PO/IM/IV):****Child:** 1–2 mg/kg/dose Q6 hr; usual dose: 5 mg/kg/24 hr  $\div$  Q6 hr. **Max. dose:** 50 mg/dose and 300 mg/24 hr**Adult:** 25–50 mg/dose Q4–8 hr; **max. dose** 400 mg/24 hr**Sleep aid (PO/IM/IV):** Administer dose 30 min before bedtime.**2–11 yr:** 1 mg/kg/dose; **max. dose** 50 mg/dose **$\geq$  12 yr:** 50 mg**Contraindicated** with concurrent MAO inhibitor use, acute attacks of asthma, and GI or urinary obstruction. **Use with caution** in infants and young children, and **do not** use in neonates, owing to potential CNS effects. Side effects include sedation, nausea, vomiting, xerostomia, blurred vision, and other reactions common to antihistamines. CNS side effects more common than GI disturbances. May cause paradoxical excitement in children. **Adjust dose in renal failure (see Chapter 31).**

**DIVALPROEX SODIUM**

Depakote, Depakote ER

**Anticonvulsant**

Yes



No



3



D/X

**Delayed-release tabs:** 125, 250, 500 mg**Extended-release tabs (Depakote ER):** 250, 500 mg**Sprinkle caps:** 125 mg**Dose:** See *Valproic Acid*

See *Valproic Acid*. Preferred over valproic acid for patients on ketogenic diet. Depakote ER is prescribed for once-daily administration, whereas Depakote is typically prescribed BID.

Depakote ER and Depakote are not bioequivalent; see package insert for dose conversion.

Efficacy was not established in separate randomized double-blinded placebo-controlled trials for the treatment of pediatric bipolar disorder (age 10–17 yr) and migraine prophylaxis (age 12–17 yr).

Pregnancy category is “X” when used for migraine prophylaxis and “D” for all other indications.

**DOBUTAMINE**

Various generics; previously available as Dobutrex

**Sympathomimetic agent**

No



No



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B

**Injection:** 12.5 mg/mL (20, 40 mL); contains sulfites**Prediluted injection in D<sub>5</sub>W:** 1 mg/mL (250 mL), 2 mg/mL (250 mL), 4 mg/mL (250 mL)**Continuous IV infusion (all ages):** 2.5–15 mcg/kg/min**Max. dose:** 40 mcg/kg/min**To prepare infusion:** See IV infusions on page i.

**Contraindicated** in idiopathic hypertrophic subaortic stenosis (IHSS). Tachycardia, arrhythmias (PVCs), and hypertension may occasionally occur (especially at higher infusion rates). Correct hypovolemic states before use. Increases AV conduction, may precipitate ventricular ectopic activity.

Dobutamine has been shown to increase cardiac output and systemic pressure in pediatric patients of every age group. However, in premature neonates, dobutamine is less effective than dopamine in raising systemic blood pressure without causing undue tachycardia, and dobutamine has not been shown to provide any added benefit when given to such infants already receiving optimal infusions of dopamine.

Monitor BP and vital signs.  $T_{1/2}$ : 2 min. Peak effects in 10–20 min. Use with linezolid may potentially increase blood pressure.

**DOCUSATE**

Colace, Kao-Tin, Sur-Q-Lax, Enemeez, and many other brands

**Stool softener, laxative**

No



No



1



C/?

**Available as docusate sodium:****Caps [OTC]:** 50, 100, 250 mg; sodium content (50 mg cap: 3 mg; 100 mg cap: ≈5 mg)**Tabs [OTC]:** 100 mg**Syrup [OTC]:** 20 mg/5 mL; may contain alcohol**Oral liquid [OTC]:** 10 mg/mL; contains 1 mg/mL sodium**Rectal enema (Enemeez [OTC]):** 283 mg/5 mL (5 mL); Enemeez Plus product contains benzocaine**Available as docusate calcium:****Caps (Kao-Tin, Sur-Q-Lax [OTC]):** 240 mg

DILTIAZEM *continued***PO: (take with liquids)****<3 yr:** 10–40 mg/24 hr ÷ once daily–QID**3–6 yr:** 20–60 mg/24 hr ÷ once daily–QID**6–12 yr:** 40–150 mg/24 hr ÷ once daily–QID**>12 yr and adult:** 50–400 mg/24 hr ÷ once daily–QID**Rectal:****Older child and adult:** Add 50–100 mg of oral liquid (not syrup) to enema fluid (saline or oil retention enemas).

Oral dosage effective only after 1–3 days of therapy. Incidence of side effects is exceedingly low. Rash, nausea, and throat irritation have been reported. Oral liquid is bitter; give with milk, fruit juice, or formula to mask taste.

A few drops of the 10 mg/mL oral liquid may be used in the ear as a cerumenolytic. Effect is usually seen within 15 min.

Pregnancy category has not been formally assigned by the FDA but is considered a “C.”

**DOLASETRON**

Anzemet

**Antiemetic agent, 5-HT<sub>3</sub> antagonist**

No



No



?



B

**Injection:** 20 mg/mL (0.625, 5, 25 mL)**Tabts:** 50, 100 mg**Oral suspension:** 10 mg/mL **Chemotherapy-induced nausea and vomiting prevention:**

**2 yr–adult:** 1.8 mg/kg/dose PO up to a **max. dose** of 100 mg. Administer PO dose 60 min before chemotherapy. IV route of administration is considered contraindicated for this indication because of increased risk for QTc prolongation.

**Postoperative nausea and vomiting prevention:** Administer IV doses 15 min before cessation of anesthesia and PO doses 2 hr before surgery.

**2–16 yr:****IV:** 0.35 mg/kg/dose (**max. dose** 12.5 mg) × 1**PO:** 1.2 mg/kg/dose × 1 (**max. dose** 100 mg) × 1**Adult:****IV:** 12.5 mg/dose × 1**PO:** 100 mg/dose × 1

**Postoperative nausea and vomiting treatment:** Administer IV at onset of nausea and vomiting.

**2–16 yr:** 0.35 mg/kg/dose (**max. dose** 12.5 mg) IV**Adult:** 12.5 mg/dose IV

May cause hypotension and prolongation of cardiac conduction intervals, particularly QTc interval (dose-dependent effect). Common side effects include dizziness, headache, sedation, blurred vision, fever, chills, and sleep disorders. Rare cases of sustained supraventricular and ventricular arrhythmias, fatal cardiac arrest, and MI have been reported in children and adolescents.

**Avoid** use in patients with congenital long QTc syndrome, hypomagnesemia, hypokalemia, or with concurrent use of other drugs that increase QTc interval (e.g., erythromycin, cisapride). Drug's active metabolite (hydrodolasetron) is a substrate for CYP 450 2D6 and 3A3/4 isoenzymes; concomitant use of enzyme inhibitors (e.g., cimetidine) may increase risk for side effects, and use of enzyme inducers (e.g., rifampin) may decrease dolasetron's efficacy. Although no dosage adjustments are necessary, hydrodolasetron's clearance decreases 42% with severe hepatic impairment and 44% with severe renal impairment.

ECG monitoring is recommended in patients with electrolyte abnormalities, CHF, or bradyarrhythmias.

IV doses may be administered undiluted over 30 sec.

**DOPAMINE**

Various generics; previously available as Intropin  
**Sympathomimetic agent**



No



No



?



C

**Injection:** 40, 80, 160 mg/mL (5, 10 mL)

**Prediluted injection in D<sub>5</sub>W:** 0.8, 1.6, 3.2 mg/mL (250, 500 mL)

**All ages:**

**Low dose:** 2–5 mcg/kg/min IV; increases renal blood flow; minimal effect on heart rate and cardiac output

**Intermediate dose:** 5–15 mcg/kg/min IV; increases heart rate, cardiac contractility, cardiac output, and to a lesser extent, renal blood flow

**High dose:** >20 mcg/kg/min IV;  $\alpha$ -adrenergic effects are prominent; decreases renal perfusion.

**Max. dose** recommended: 20–50 mcg/kg/min IV

**To prepare infusion:** See IV infusions on page i.

**Do not** use in pheochromocytoma, tachyarrhythmias, or hypovolemia. Monitor vital signs and blood pressure continuously. Correct hypovolemic states. Tachyarrhythmias, ectopic beats, hypertension, vasoconstriction, and vomiting may occur. **Use with caution** with phenytoin; hypotension and bradycardia may be exacerbated. Use with linezolid may potentially increase blood pressure.

Newborn infants may be more sensitive to vasoconstrictive effects of dopamine. Children <2 yr of age clear dopamine faster and exhibit high variability in neonates.

Should be administered through a central line or large vein. Extravasation may cause tissue necrosis; treat with phentolamine. **Do not** administer into an umbilical arterial catheter.

**DORNASE ALFA/DNASE**

Pulmozyme

**Inhaled mucolytic**



No



No



?



B

Inhalation solution: 1 mg/mL (2.5 mL)

**Cystic fibrosis:**

**Child > 5 yr and adult:** 2.5 mg via nebulizer once daily. Some patients may benefit from 2.5 mg BID.

**Contraindicated** in patients with hypersensitivity to epoetin alfa. Voice alteration, pharyngitis, laryngitis may result. These are generally reversible without dose adjustment. Safety and efficacy has not been demonstrated in patients >1 year of continuous use.

**Do not** mix with other nebulized drugs. A  $\beta$ -agonist may be useful before administration to enhance drug distribution. Chest physiotherapy should be incorporated into treatment regimen. The following nebulizer compressor systems have been recommended for use: Pulmo-Aide, Pari-Proneb, Mobilair, Porta-Neb, or PariBaby. Use of the “Sidestream” nebulizer cup can significantly reduce medication administration time.

**DOXAPRAM HCL**

Dopram and generics

**CNS stimulant**

No



No



?



B

**Injection:** 20 mg/mL (20 mL); may contain 0.9% benzyl alcohol**Methylxanthine-refractory neonatal apnea:** Load with 2.5–3 mg/kg over 15 min, followed by a continuous infusion of 1 mg/kg/hr titrated to lowest effective dose; **max. dose** 2.5 mg/kg/hr**Contraindicated** in seizures, proven or suspected pulmonary embolism, head injuries, cerebral vascular accident, cerebral edema, cardiovascular or coronary artery disease, severe hypertension, pheochromocytoma, hyperthyroidism, and in patients with mechanical disorders of ventilation. **Do not** use with general anesthetic agents that can sensitize the heart to catecholamines (e.g., halothane, cyclopropane, enflurane) to reduce risk of cardiac arrhythmias, including ventricular tachycardia and ventricular fibrillation. **Do not** initiate doxapram until general anesthetic agent has been completely excreted.Hypertension occurs with higher doses (>1.5 mg/kg/hr). May also cause tachycardia, arrhythmias, seizure, hyperreflexia, hyperpyrexia, abdominal distension, bloody stools, and sweating. **Avoid** extravasation into tissues.**DOXYCYCLINE**

Adoxa, Vibramycin, Periostat, Doryx, many others, and generics

**Antibiotic, tetracycline derivative**

Yes



Yes



2



D

**Caps:** 20 (Periostat), 50, 75, 100, 150 mg**Tab:** 20 (Periostat), 50, 75, 100, 150 mg

Delayed-release caps: 40, 100 mg

Delayed-release tabs (Doryx): 80, 100, 150, 200 mg

**Syrup:** 50 mg/5 mL (60 mL); contains parabens**Oral suspension:** 25 mg/5 mL (60 mL)**Injection:** 100 mg**Initial:****≤45 kg:** 2.2 mg/kg/dose BID PO/IV × 1 day to **max. dose** of 200 mg/24 hr**>45 kg:** 100 mg/dose BID PO/IV × 1 day**Maintenance:****≤45 kg:** 2.2–4.4 mg/kg/24 hr once daily–BID PO/IV**>45 kg:** 100–200 mg/24 hr ÷ once daily–BID PO/IV**Max. dose:** 200 mg/24 hr**PID:****Inpatient:** 100 mg Q12 hr with cefotetan or cefoxitin, or ampicillin/sulbactam. Convert to oral therapy 24 hr after patient improves on IV to complete a 14-day total course (IV and PO).**Outpatient:** 100 mg PO Q12 hr × 14 days with ceftriaxone, cefoxitin + probenecid, or other parenteral third-generation cephalosporin with or without metronidazole.**Anthrax (inhalation/systemic/cutaneous [see remarks]):** Initiate therapy with IV route, and convert to PO route when clinically appropriate. Duration of therapy is 60 days (IV and PO combined):**≤8 yr or ≤45 kg:** 2.2 mg/kg/dose BID IV/PO; **max. dose** 200 mg/24 hr**>8 yr and >45 kg:** 100 mg/dose BID IV/PO

Continued

DOXYCYCLINE *continued*

**Malaria prophylaxis (start 1–2 days before exposure, and continue for 4 wk after leaving endemic area):**

**>8 yr:** 2 mg/kg/24 hr PO once daily; **max. dose** 100 mg/24 hr and **max. duration** of 4 mo

**Adult:** 100 mg PO once daily

**Periodontitis:**

**Adult:** 20 mg BID PO  $\times \leq 9$  mo

**Use with caution** in hepatic and renal disease. Generally **not recommended** for use in children <8 yr owing to risk for tooth enamel hypoplasia and discoloration. However, the AAP *Redbook* recommends doxycycline as the drug of choice for rickettsial disease regardless of age. May cause GI symptoms, photosensitivity, hemolytic anemia, rash, and hypersensitivity reactions. Increased intracranial pressure (pseudotumor cerebri), TEN, erythema multiforme, and Stevens-Johnson syndrome have been reported.

Doxycycline is approved for treatment of anthrax (*Bacillus anthracis*) in combination with one or two other antimicrobials. If meningitis is suspected, consider using an alternative agent because of poor CNS penetration. Consider changing to high-dose amoxicillin (25–35 mg/kg/dose TID PO) for penicillin-susceptible strains. See [www.bt.cdc.gov](http://www.bt.cdc.gov) for the latest information.

Rifampin, barbiturates, phenytoin, and carbamazepine may increase clearance of doxycycline.

Doxycycline may enhance the hypoprothrombinemic effect of warfarin. See *Tetracycline* for additional drug/food interactions and remarks.

Infuse IV over 1–4 hr. **Avoid** prolonged exposure to direct sunlight.

For periodontitis, take capsules  $\geq 1$  prior to meals, and take tablets  $\geq 1$  hr before or 2 hr after meals.

**DRONABINOL**

Marinol, Tetrahydrocannabinol, THC, and generics

**Antiemetic**



Yes



No



X



C

**Caps:** 2.5, 5, 10 mg; may contain sesame oil

**Antiemetic:**

**Child and adult (PO):** 5 mg/m<sup>2</sup>/dose 1–3 hr before chemotherapy, then Q2–4 hr up to a **max. dose** of 6 doses/24 hr; doses may be gradually increased by 2.5 mg/m<sup>2</sup>/dose increments up to a **max. dose** of 15 mg/m<sup>2</sup>/dose if needed and tolerated.

**Appetite stimulant:**

**Adult (PO):** 2.5 mg BID 1 hr before lunch and dinner; if not tolerated, reduce dose to 2.5 mg QHS.

**Max. dose:** 20 mg/24 hr (**use caution** when increasing doses because of increased risk of dose-related adverse reactions at higher dosages).

**Contraindicated** in patients with history of substance abuse, mental illness, or allergy to sesame oil. **Use with caution** in heart disease, seizures, hepatic disease (reduce dose if severe). Side effects: euphoria, dizziness, difficulty concentrating, anxiety, mood change, sedation, hallucinations, ataxia, paresthesia, hypotension, excessively increased appetite, and habit-forming potential.

Onset of action: 0.5–1 hr; duration of psychoactive effects, 4–6 hr; appetite stimulation, 24 hr.

**DROPERIDOL**

Inapsine and generics

**Sedative, antiemetic**

Yes



Yes



3



C

**Injection:** 2.5 mg/mL (2 mL)**Antiemetic/sedation:****Child:** 0.03–0.07 mg/kg/dose IM or IV over 2–5 min; if needed, may give 0.1–0.15 mg/kg/dose; initial **max. dose** 0.1 mg/kg/dose, and subsequent **max. dose** 2.5 mg/dose.**Dosage interval:****Antiemetic:** PRN Q4–6 hr.**Sedation:** Repeat dose in 15–30 min if necessary.**Adult:** 2.5–5 mg IM or IV over 2–5 min; initial **max. dose** is 2.5 mg.**Dosage interval:****Antiemetic:** PRN Q3–4 hr.**Sedation:** Repeat dose in 15–30 min if necessary.

**Use with caution** in renal and hepatic impairment; 75% of metabolites are excreted renally, and drug is extensively metabolized in the liver. Side effects include hypotension, tachycardia, extrapyramidal side effects, such as dystonia, feeling of motor restlessness, laryngospasm, bronchospasm. May lower seizure threshold. **Fatal arrhythmias and QT interval prolongation has been associated with use.**

Onset in 3–10 min. Peak effects within 10–30 min. Duration: 2–4 hr. Often given as adjunct to other agents.

**EDETATE (EDTA) CALCIUM DISODIUM**

Calcium disodium versenate and generics

**Chelating agent, antidote for lead toxicity**

Yes



Yes



?



B

**Injection:** 200 mg/mL (5 mL)**Lead poisoning:****Lead level > 70 mcg/dL (use with dimercaprol):** Initiate at the time of the second dimercaprol dose, and treat for 3–5 days. May repeat a course as needed after 2–4 days of no EDTA.**IM:** 1000–1500 mg/m<sup>2</sup>/24 hr ÷ Q4 hr**IV:** 1000–1500 mg/m<sup>2</sup>/24 hr as an 8–24 hour infusion or divided Q12 hrUse 1500 mg/m<sup>2</sup>/24 hr for 5 days in the presence of encephalopathy.**Lead level 20–70 mcg/dL:** 1000 mg/m<sup>2</sup>/24 hr IV as an 8–24 hr infusion *OR* intermittent dosing divided Q12 hr × 5 days. May repeat course as needed after 2–4 days of no EDTA.**Max. daily dose:** 75 mg/kg/24 hr

**Edetate (EDTA) calcium disodium is NOT interchangeable with edetate disodium (Na<sub>2</sub>EDTA); erroneous substitutions have led to fatalities.** Prescribe this product by its full name and **avoid** the EDTA abbreviation to prevent dispensing errors.

May cause renal tubular necrosis. **Do not use** in the presence of anuria, hepatitis, and active renal disease. Dosage reduction is recommended with mild renal disease. Follow urinalysis and renal function. Monitor ECG continuously for arrhythmia when giving IV. Rapid IV infusion may cause sudden increase in intracranial pressure in patients with cerebral edema. May cause zinc and copper deficiency. Monitor Ca<sup>2+</sup> and PO<sub>4</sub>.

IM route preferred. Give IM with 0.5% procaine.



**EDROPHONIUM CHLORIDE**

Enlon, Tensilon

**Anticholinesterase agent, antidote for neuromuscular blockade**

No



Yes



?



?

**Injection:** 10 mg/mL (15 mL) (contains 0.45% phenol and 0.2% sulfite)**Diagnosis for myasthenia gravis (IV [see remarks]):****Neonate:** 0.1 mg single dose**Infant and child:****Initial:** 0.04 mg/kg/dose  $\times$  1**Max. dose:** 1 mg for <34 kg, 2 mg for  $\geq$ 34 kg

If no response after 1 min, may give 0.16 mg/kg/dose for a total of 0.2 mg/kg.

**Total max. dose:** 5 mg for <34 kg, 10 mg for  $\geq$ 34 kg**Adult:** 2-mg test dose IV; if no reaction, give 8 mg after 45 sec.

May precipitate cholinergic crisis, arrhythmias, and bronchospasm. Keep atropine available in syringe, and have resuscitation equipment ready. Hypersensitivity to test dose (fasciculations or intestinal cramping) is indication to stop giving drug. **Contraindicated** in GI or GU obstruction, or arrhythmias. Dose may have to be reduced in chronic renal failure.

Reported doses for reversing neuromuscular blockade in children have ranged from 0.1–1.43 mg/kg/dose.

Antagonism of nondepolarizing neuromuscular blocking drugs in children is more rapid than in adults.

Short duration of action with IV route (5–10 min). **Antidote:** atropine 0.01–0.04 mg/kg/dose.

Pregnancy category has not been established.

**EMLA**

See Lidocaine and Prilocaine

**ENALAPRIL MALEATE (PO), ENALAPRILAT (IV)**

Enalapril: Vasotec, Epaned, and other generics

Enalaprilat: Vasotec IV and other generics

**Angiotensin-converting enzyme inhibitor, antihypertensive**

No



Yes



2



D

**Enalapril:**

Tabs: 2.5, 5, 10, 20 mg

Oral suspension: 0.1, 1 mg/mL

**Epaned:** 1 mg/mL (150 mL); contains parabens and saccharin**Enalaprilat:**

Injection: 1.25 mg/mL (1, 2 mL); contains benzyl alcohol

**Hypertension:****Infant and child:****PO:** 0.08 mg/kg/24 hr up to 5 mg/24 hr  $\div$  once daily; increase PRN over 2 wk**Max. dose** (higher doses have not been evaluated): 0.58 mg/kg/24 hr up to 40 mg/24 hr**IV:** 0.005–0.01 mg/kg/dose Q8–24 hr; **max. dose** 1.25 mg/dose**Adolescent and adult:****PO:** 2.5–5 mg/24 hr once daily initially to **max. dose** of 40 mg/24 hr  $\div$  once daily–BID**IV:** 0.625–1.25 mg/dose IV Q6 hr; doses as high as 5 mg Q6 hr are reported to be tolerated for up to 36 hr.

**Use with caution** in bilateral renal artery stenosis. **Avoid use** with dialysis with high-flux membranes; anaphylactoid reactions have been reported. Side effects: nausea, diarrhea, headache, dizziness, hyperkalemia, hypoglycemia, hypotension, and hypersensitivity. Cough is a reported side effect of ACE inhibitors.



ENALAPRIL MALEATE (PO), ENALAPRILAT (IV) *continued*

Enalapril (PO) is converted to its active form (Enalaprilat) by the liver. Administer IV over 5 min. **Adjust dose in renal impairment (see Chapter 31).**

Nitritoid reactions have been in patients receiving concomitant IV gold therapy. Enalapril/enalaprilat should be discontinued as soon as possible when pregnancy is detected. If oliguria or hypotension occurs in a neonate with in utero exposure to enalapril/enalaprilat, exchange transfusions or dialysis may be necessary to reverse hypotension and/or support renal function.

### ENOXAPARIN

Lovenox and generics

**Anticoagulant, low-molecular-weight heparin**



Yes



Yes



2



B

**Injection:** 100 mg/mL (3 mL); contains 15 mg/mL benzyl alcohol

**Injection (prefilled syringes with 27-gauge, ½-inch needle):** 30 mg/0.3 mL, 40 mg/0.4 mL, 60 mg/0.6 mL, 80 mg/0.8 mL, 100 mg/1 mL, 120 mg/0.8 mL, 150 mg/1 mL

**Approximate anti-factor Xa activity:** 100 IU per 1 mg

Initial empirical dosage; patient-specific dosage defined by therapeutic drug monitoring when indicated (see remarks).



#### DVT treatment:

**Infant < 2 mo:** 1.5 mg/kg/dose Q12 hr SC

**Infant ≥ 2 mo–adult:** 1 mg/kg/dose Q12 hr SC; alternatively, 1.5 mg/kg/dose Q24 hr SC can be used in adults.

**Dosage adjustment for DVT treatment to achieve target anti-factor Xa low-molecular-weight heparin (LMWH) levels of 0.5–1 units/mL (see following table):**

Anti-Factor Xa Level LMWH (units/mL)	Hold Next Dose?	Dose Change	Repeat Anti-Factor Xa Level LMWH?
<0.4	No	Increase by 25%	4 hr post next new dose
0.4	No	Increase by 10%	4 hr post next new dose
0.5	No	No	4 hr post next dose; if within therapeutic range, recheck 1 week later at 4 hr post dose
0.6–0.7	No	No	1 week later at 4 hr post dose
0.8–1	No	No	4 hr post next dose; if within therapeutic range, recheck 1 week later at 4 hr post dose
1.1–1.5	No	Decrease by 20%	4 hr post next new dose
1.6–2	3 hr	Decrease by 30%	Trough level (goal: <0.5) before next new dose and 4 hr post next new dose
>2	Until anti-factor Xa LMWH reaches 0.5 units/mL (levels can be measured Q12 hr until it reaches ≤0.5 units/mL).	When anti-factor Xa LMWH reaches 0.5 units/mL, dose may be restarted at a dose 40% less than originally prescribed.	4 hr post next new dose

*Continued*

ENOXAPARIN *continued***DVT prophylaxis:****Infant < 2 mo:** 0.75 mg/kg/dose Q12 hr SC**Infant ≥ 2 mo–child 18 yr:** 0.5 mg/kg/dose Q12 hr SC; **max. dose** 30 mg/dose**Patients with indwelling epidural catheters/neuraxial anesthesia (≥2 mo–child 18 yr):** 1 mg/kg/dose Q24 hr SC; **max. dose** 40 mg/dose. Twice-daily dosing is **contraindicated** for these patients.

See remarks.

Adjust dosage for DVT prophylaxis to achieve target anti–factor Xa levels of 0.1–0.3 units/mL for all children.

**Adult:****Knee or hip replacement surgery:** 30 mg BID SC × 7–14 days; initiate therapy 12–24 hr after surgery, provided hemostasis is established. Alternatively for hip replacement surgery, 40 mg once daily SC × 7–14 days initially up to 3 wk thereafter; initiate therapy 9–15 hr before surgery.**Abdominal surgery:** 40 mg once daily SC × 7–12 days initiated 2 hr before surgery.**Patients at risk due to severe restricted mobility during an acute illness:** 40 mg once daily SC × 6–14 days.

Inhibits thrombosis by inactivating factor Xa without significantly affecting bleeding time, platelet function, PT, or APTT at recommended doses. Dosages of enoxaparin, heparin, or other LMWHs **cannot** be used interchangeably on a unit-for-unit (or mg-for-mg) basis because of differences in pharmacokinetics and activity. Peak anti–factor Xa LMWH activity is achieved 4 hr after a dose. **Anti–factor Xa LMWH is NOT THE SAME as unfractionated heparin anti–Xa level (used for monitoring heparin therapy).**



**Contraindicated** in major bleeding and drug-induced thrombocytopenia. **Use with caution** in uncontrolled arterial hypertension, bleeding diathesis, history of recurrent GI ulcers, diabetic retinopathy, and severe renal dysfunction (reduce dose by increasing dosage interval from Q12 hr to Q24 hr if GFR < 30 mL/min). Prophylactic use not recommended in patients with prosthetic heart valves (especially pregnant women) because of reports of fatalities in patients and fetuses.

**Concurrent use with spinal or epidural anesthesia or spinal puncture has resulted in long-term or permanent paralysis; potential benefits must be weighed against risks.** May cause fever, confusion, edema, nausea, hemorrhage, thrombocytopenia, hypochromic anemia, and pain/erythema at injection site. Allergic reactions, headache, eosinophilia, alopecia, hepatocellular and cholestatic liver injury, and osteoporosis (long-term use) have been reported. **Protamine sulfate is the antidote;** 1 mg protamine sulfate neutralizes 1 mg enoxaparin.

DVT prophylaxis for patients with epidural catheters/neuraxial anesthesia: If placing needle, hold anticoagulation for 12 hr, and restart dosing no sooner than 4 hr after needle insertion. If removing catheter, hold anticoagulation for 12 hr, and restart dosing no sooner than 2 hr after catheter removal.

Recommended anti–factor Xa LMWH levels obtained 4 hr after subcutaneous dose after the third consecutive dose:

DVT treatment: 0.5–1 units/mL

DVT prophylaxis: 0.1–0.3 units/mL

Administer by deep SC injection by having patient lie down. Alternate administration between the left and right anterolateral and left and right posterolateral abdominal wall. See package insert for detailed SC administration recommendations. To minimize bruising, do not rub the injection site. IV or IM route of administration is not recommended.

For additional information, see *Chest*. 2008;133:887-968 and *Regional Anesth Pain Med*. 2003;28:172-197.

**EPINEPHRINE HCL**

Adrenalin, EpiPen, other brand names and generics

**Sympathomimetic agent**

No



No



?



C

**Injection:**

1:1000 (aqueous): 1 mg/mL (1, 30 mL)

1:10,000 (aqueous): 0.1 mg/mL (10 mL prefilled syringes with either 18G, 3.5-inch or 21G, 1.5-inch needles or 10-mL vials)

**Autoinjector:**

EpiPen and others: Delivers a single 0.3-mg (0.3-mL) dose (1 or 2 pack)

EpiPen Jr and others: Delivers a single 0.15-mg (0.3-mL) dose (1 or 2 pack)

Some preparations may contain sulfites.

**Cardiac uses:****Neonate:****Asystole and bradycardia:** 0.01–0.03 mg/kg of 1:10,000 solution (0.1–0.3 mL/kg) IV/ET Q3–5 min PRN**Infant and child:****Bradycardia/asystole and pulseless arrest:** See page ii and PALS algorithms in back of book.**Bradycardia, asystole, and pulseless arrest (see remarks):****First dose:** 0.01 mg/kg of 1:10,000 solution (0.1 mL/kg) IO/IV; **max. dose** 1 mg (10 mL).

Subsequent doses Q3–5 min PRN should be the same. High-dose epinephrine after failure of standard dose has not been shown to be effective (see remarks). Must circulate drug with CPR. For ET route see below.

**All ET doses:** 0.1 mg/kg of 1:1000 solution (0.1 mL/kg) ET Q3–5 min**Adult:****Asystole:** 1–5 mg IV/ET Q3–5 min**IV drip (all ages):** 0.1–1 mcg/kg/min; titrate to effect; to prepare infusion, see inside front cover.**Respiratory uses:****Bronchodilator:** 1:1000 (aqueous):**Infant and child:** 0.01 mL/kg/dose SC (**max. single dose** 0.5 mL); repeat Q15 min  $\times$  3–4 doses or Q4 hr PRN**Adult:** 0.3–0.5 mg (0.3–0.5 mL)/dose SC Q20 min  $\times$  3 doses**Nebulization (alternative to racemic epinephrine):** 0.5 mL/kg of 1:1000 solution diluted in 3 mL NS. **Max. doses:**  $\leq$ 4 yr, 2.5 mL/dose;  $>$ 4 yr, 5 mL/dose**Hypersensitivity reactions (see remarks for IV dosing):****Child:** 0.01 mg/kg/dose IM/SC up to a **max. dose** of 0.5 mg/dose Q20 min–4 hr PRN. If using EpiPen or EpiPen Jr, administer only via IM route using following dosage:**<30 kg:** 0.15 mg **$\geq$ 30 kg:** 0.3 mg**Adult:** Start with 0.1–0.5 mg IM/SC Q20 min–4 hr PRN; doses may be increased if necessary to a single **max. dose** of 1 mg.High-dose rescue therapy for in-hospital cardiac arrest in children after failure of an initial standard dose has been reported to be of no benefit compared to standard dose (*N Engl J Med.* 2004;350:1722–1730).**Hypersensitivity reactions:** For bronchial asthma and certain allergic manifestations (e.g., angioedema, urticaria, serum sickness, anaphylactic shock) use epinephrine SC. Patients with anaphylaxis may benefit from IM administration. Adult IV dose for hypersensitivity reactions or to relieve bronchospasm usually ranges from 0.1–0.25 mg injected slowly over 5–10 min Q5–15 min as needed. Neonates may be given a dose of 0.01 mg/kg body weight; for infants, 0.05 mg is an adequate initial dose, and this may be repeated at 20- to 30-min intervals in the management of asthma attacks.

Continued

EPINEPHRINE HCL *continued*

May produce arrhythmias, tachycardia, hypertension, headaches, nervousness, nausea, vomiting.

Necrosis may occur at site of repeated local injection.

Concomitant use of noncardiac selective  $\beta$ -blockers or tricyclic antidepressants may enhance epinephrine's pressor response. Chlorpromazine may reverse pressor response.

ETT doses should be diluted with NS to a volume of 3–5 mL before administration. Follow with several positive-pressure ventilations.

EpiPen and EpiPen Jr should be administered IM into anterolateral aspect of thigh. See EpiPen product information for proper use of the device and to prevent injury and/or inadvertent dose administration to the individual administering the dose. Accidental injection into digits, hands, or feet may result in loss of blood flow to affected area.

**EPINEPHRINE, RACEMIC**

S-2 Inhalant and others

**Sympathomimetic agent**



No



No



?



C

**Solution for inhalation (OTC):** 2.25% (1.25% epinephrine base) (0.5, 15, 30 mL)

Contains edetate disodium and may contain sulfites

**<4 yr:**

**Croup (using 2.25% solution):** 0.05 mL/kg/dose up to a **max. dose** of 0.5 mL/dose, diluted to 3 mL with NS. Given via nebulizer over 15 min PRN but **not** more frequently than Q1–2 hr.

**≥4 yr:** 0.5 mL/dose diluted to 3 mL with NS via nebulizer over 15 min Q3–4 hr PRN



Tachyarrhythmias, headache, nausea, palpitations reported. Rebound symptoms may occur.

Cardiorespiratory monitoring should be considered if administered more frequently than Q1–2 hr.

**EPOETIN ALFA**

Erythropoietin, Epogen, Procrit

**Recombinant human erythropoietin**



No



No



2



C

**Injection (single-dose, preservative-free vials):** 2000, 3000, 4000, 10,000, 40,000 U/mL (1 mL)

**Injection (multidose vials):** 10,000 U/mL (2 mL), 20,000 U/mL (1 mL); contains 1% benzyl alcohol

All dosage forms contain 2.5 mg albumin per 1 mL.

**Anemia in chronic renal failure (see remarks for dosage adjustment and withholding therapy):** SC/IV (IV preferred for hemodialysis patients)



**Initial dose:**

**Child and adolescent:** Start at 50 U/kg/dose 3 times per week. Reported dosage range for children (3 mo–20 yr) not requiring dialysis, 50–250 U/kg/dose 3 times per week. Reported dosage range for children receiving hemodialysis, 50–450 U/kg/dose 2–3 times per week.

**Adult:** Start at 50–100 U/kg/dose 3 times per week.

**Maintenance dose:** Dose is individualized to achieve and maintain the lowest Hgb level sufficient to avoid transfusions and **not to exceed** 11 g/dL.

**Anemia in cancer (use until chemotherapy is completed; see remarks for dosage reduction and withholding therapy):**

**Initial dose:**

**Child (5–18 yr):** Start at 600 U/kg (**max. dose** 40,000 U) IV once weekly.

**Adult:** Start at 150 U/kg/dose SC 3 times per week or 40,000 U SC once every week.

EPOETIN ALFA *continued***Increasing doses (if needed):**

**Three-times-a-week dosing regimen (adult):** If no increase in Hgb >1 g/dL, and Hgb remains <10 g/dL after initial 4 wk of therapy, increase dosage to 300 U/kg/dose 3 times per week.

**Weekly dosing regimen:** If no increase in Hgb >1 g/dL, and Hgb remains <10 g/dL after initial 4 wk of therapy:

**Child:** Increase dose to 900 U/kg/dose IV (**max. dose** 60,000 U) once weekly

**Adult:** 60,000 U SC once weekly

**For all ages,** discontinue use after 8 wk of therapy if transfusions are still required or no hemoglobin response is observed.

**AZT-treated HIV patients (Hgb should not exceed 12 g/dL):** SC/IV

**Child:** Reported dosage range in children (8 mo–17 yr), 50–400 U/kg/dose 2–3 times per wk.

**Adult (with serum erythropoietin  $\leq 500$  milliunits/mL and receiving  $\leq 4200$  mg AZT per week):** Start at 100 U/kg/dose 3 times per wk  $\times$  8 wk.

**Dose increments (if needed):** If response is not satisfactory in reducing transfusion requirements or increasing Hgb levels after 8 wk of therapy, dose may be increased by 50–100 U/kg/dose given 3 times per wk, and reevaluate every 4–8 wk thereafter. Patients are unlikely to respond to doses >300 U/kg/dose 3 times per wk.

**For all ages,** withhold therapy if Hgb > 12 g/dL, and resume therapy by decreasing dosage by 25% once Hgb falls below 11 g/dL. For adults, discontinue therapy if Hgb does not increase after 8 wk of the 300 U/kg/dose 3 times per wk.

**Anemia of prematurity (many regimens exist):**

250 U/kg/dose SC 3 times per wk  $\times$  10 doses; alternatively, 200–400 U/kg/dose IV/SC 3–5 times per wk for 2–6 wk (total dose per wk is 600–1400 U/kg). Administer with supplemental iron at 3–6 mg elemental iron/kg/24 hr.

Use the lowest dose to avoid transfusions. Increased risk for death, serious cardiovascular events, and thrombosis/stroke have been reported in patients treated with chronic kidney disease and hemoglobin levels > 11 g/dL. Increased risk for death, shortened survival and/or shortened time to tumor progression/regression, serious cardiovascular events, and thrombosis in various cancer patients, especially with Hgb levels >12 g/dL, have been reported with epoetin alfa and other erythropoiesis-stimulating agents.

Evaluate serum iron, ferritin, TIBC before therapy. Iron supplementation recommended during therapy unless iron stores are already in excess. Monitor Hct, BP, clotting times, platelets, BUN, serum creatinine. Peak effect in 2–3 wk.

**DOSAGE ADJUSTMENT FOR ANEMIA IN CHRONIC RENAL FAILURE:**

**Reduce dose by  $\geq 25\%$ :** when Hgb increases >1 g/dL in any 2-wk period. Dose reductions can be made more frequently than once every 4 weeks if needed.

**Increase dose by 25%:** when Hgb does not increase by 1 g/dL after 4 wk of therapy. Dosage increments should not be made more frequently than once every 4 wk.

**Withholding therapy:** When Hgb > 11 g/dL; restart therapy at a 25% lower dose after Hgb decreases to target levels or <11 g/dL.

**Inadequate response after a 12-week dose escalation:** Use minimum effective dosage that will maintain Hgb levels to avoid the need for recurrent blood transfusions, and evaluate other causes of anemia. Discontinue use if patient remains transfusion dependent.

**DOSAGE REDUCTION ADJUSTMENT/WITHHOLDING THERAPY FOR ANEMIA IN CANCER:**

**If Hgb exceeds a level needed to avoid blood transfusion:** Withhold dose and resume therapy at a reduced dosage by 25% when Hgb approaches a level where blood transfusions may be needed.

**If Hgb increases >1 g/dL in any 2-wk period or Hgb reaches a level to avoid blood transfusion:** Reduce dose by 25%.

May cause hypertension, seizure, hypersensitivity reactions, headache, edema, dizziness. SC route provides sustained serum levels compared to IV route. For IV administration, infuse over 1–3 min. Do not use multidose vial preparation for breast-feeding mothers because of concerns for benzyl alcohol.



**ERGOCALCIFEROL**

Drisdol, Calciferol, Calcidol, and other generics

**Vitamin D<sub>2</sub>**

No



No



2



A/C

**Caps:** 50,000 IU (1.25 mg)**Tabs:** 400, 2000 IU**Drops [OTC]:** 8000 IU/mL (200 mcg/mL) (60 mL); contains propylene glycol

1 mg = 40,000 IU vitamin D activity

**Dietary supplementation** (see Chapter 21 for additional information):**Preterm:** 400–800 IU/24 hr PO**Infant (<1 yr):** 400 IU/24 hr PO**Child (≥1 yr) and adolescent:** 600 IU/24 hr PO**Renal failure (CKD stages 2–5) and 25-OH vitamin D levels < 30 ng/mL** (monitor serum 25-OH vitamin D and corrected calcium/phosphorus 1 mo after initiation and Q3 mo thereafter):**25-OH vitamin D < 5 ng/mL:****Child:** 8000 IU/24 hr × 4 wk, followed by 4000 IU/24 hr × 2 mo; **OR** 50,000 IU weekly × 4 wk, followed by 50,000 IU twice monthly for 2 mo**25-OH vitamin D 5–15 ng/mL:****Child:** 4000 IU/24 hr PO × 12 wk **OR** 50,000 IU every other wk × 12 wk**25-OH vitamin D 16–30 ng/mL:****Child:** 2000 IU/24 hr PO × 3 mo **OR** 50,000 IU every mo × 3 mo**Vitamin D–dependent rickets:****Child:** 3000–5000 IU/24 hr PO; **max. dose** 60,000 IU/24 hr**Nutritional rickets:****Child and adult with normal GI absorption:** 2000–5000 IU/24 hr PO × 6–12 week**Malabsorption:****Child:** 10,000–25,000 IU/24 hr PO**Adult:** 10,000–300,000 IU/24 hr PO**Vitamin D–resistant rickets (with phosphate supplementation):****Child:** initial dose 40,000–80,000 IU/24 hr PO; increase daily dose by 10,000–20,000 IU PO Q3–4 mo if needed.**Adult:** 10,000–60,000 IU/24 hr PO**Hypoparathyroidism (with calcium supplementation):****Child:** 50,000–200,000 IU/24 hr PO**Adult:** 25,000–200,000 IU/24 hr PO

Monitor serum Ca<sup>2+</sup>, PO<sub>4</sub>, 25-OH vitamin D (goal level for infant and child: ≥20 ng/mL), and alkaline phosphatase. Serum Ca<sup>2+</sup>, PO<sub>4</sub> product should be <70 mg/dL to avoid ectopic calcification. Titrate dosage to patient response. Watch for symptoms of hypercalcemia: weakness, diarrhea, polyuria, metastatic calcification, nephrocalcinosis. Vitamin D<sub>2</sub> is activated by 25-hydroxylation in liver and 1-hydroxylation in kidney.

Serum 25-OH vitamin D level of ≥35 ng/mL has been suggested in cystic fibrosis patients to decrease risk of hyperparathyroidism and bone loss.

Pregnancy category changes to "C" if used in doses above U.S. RDA.



**ERGOTAMINE TARTRATE ± CAFFEINE**

Ergomar

In combination with caffeine: Cafergot, Migergot and other generics

**Ergot alkaloid**

Yes



Yes



X



X

Sublingual tabs (Ergomar): 2 mg

**In combination with caffeine:**

Tabs: 1 mg and 100 mg caffeine

Suppository: 2 mg and 100 mg caffeine (12s)

**Doses based on mg of ergotamine.****Older child and adolescent:****PO/SL:** 1 mg at onset of migraine attack, then 1 mg Q30 min PRN up to **max. dose** of 3 mg per 24 hr; **do not exceed** 5 mg per wk.**Adult:****PO/SL:** 2 mg at onset of migraine attack, then 1–2 mg Q30 min up to 6 mg per 24 hr; **do not exceed** 10 mg per wk.**Suppository:** 2 mg at first sign of attack; follow with second 2-mg dose after 1 hr; **max. dose** 4 mg per 24 hr, **not to exceed** 10 mg/wk.

**Use with caution** in renal or hepatic disease. May cause paresthesias, GI disturbance, angina-like pain, rebound headache with abrupt withdrawal, or muscle cramps. **Contraindicated** in pregnancy and has **not been recommended** in breast-feeding. Concurrent administration with protease inhibitors, clarithromycin, erythromycin, or other CYP 450 3A4 inhibitors is contraindicated owing to risk of ergotism (nausea, vomiting, vasospastic ischemia leading to cerebral and peripheral ischemia).

**ERTAPENEM**

Invanz

**Antibiotic, carbapenem**

No



Yes



2



B

Injection: 1 g

Contains ≈ 6 mEq Na/g drug

**3 mo–12 yr:** 15 mg/kg/dose IV/IM Q12 hr; **max. dose** 1 g/24 hr**Adolescent and adult:** 1 g IV/IM Q24 hr**Recommended duration of therapy (all ages):****Complicated intraabdominal infection:** 5–14 days**Complicated skin/subcutaneous tissue infections:** 7–14 days**Diabetic foot infection without osteomyelitis:** up to 28 days**Community-acquired pneumonia, complicated UTI/pyelonephritis:** 10–14 days**Acute pelvic infection:** 3–10 days**Surgical site prophylaxis for colorectal surgery:** 1 g IV 1 hr before procedure

Ertapenem has poor activity against *Pseudomonas aeruginosa*, *Acinetobacter*, MRSA, and *Enterococcus*. **Do not use** in meningitis; has poor CSF penetration. **Use with caution** with CNS disorders, including seizures. Adjust dosage in renal impairment; see Chapter 31.

Diarrhea, infusion complications, nausea, headache, vaginitis, phlebitis/thrombophlebitis, and vomiting are common. Seizures (primarily with renal insufficiency and/or CNS disorders such as brain lesions and seizures), muscle weakness, gait disturbance, abnormal coordination, and DRESS syndrome have been reported. Increased ALT, AST, and neutropenia have been reported in pediatric clinical trials. Decreases valproic acid levels. Probenecid may increase ertapenem levels.

IM route requires reconstitution with 1% lidocaine and **should not** be administered IV. **Do not** reconstitute or co-infuse with dextrose-containing solutions.



**ERYTHROMYCIN ETHYLSUCCINATE AND ACETYSULFISOXAZOLE**

Pediazole, E.S.P., and other generics

**Antibiotic, macrolide + sulfonamide derivative**

Yes



Yes



2



C/D

**Oral suspension:** 200 mg erythromycin and 600 mg sulfisoxazole/5 mL (100, 150, 200, 250 mL)**Otitis media:** $\geq 2$  mo: 50 mg/kg/24 hr (as erythromycin) and 150 mg/kg/24 hr (as sulfisoxazole)  $\div$  Q6–8 hr PO, *OR* give 1.25 mL/kg/24 hr  $\div$  Q6–8 hr PO**Max. dose:** 2 g erythromycin, 6 g sulfisoxazole/24 hr**Adult:** 400 mg erythromycin and 1200 mg sulfisoxazole Q6 hr PO**Contraindicated** in liver dysfunction or porphyria. See adverse effects and drug interactions of *Erythromycin* and *Sulfisoxazole*. **Not recommended** in infants <2 mo. **Do not use** in renal impairment because dosage adjustments are inconsistent for sulfisoxazole and erythromycin. Pregnancy category changes to "D" if administered near term.**ERYTHROMYCIN PREPARATIONS**

Erythrocin, Pediaamycin, E-Mycin, Ery-Ped, EES, and other generics

**Ophthalmic ointment:** Ilotycin, Romycin, and others**Antibiotic, macrolide**

Yes



Yes



2



B

**Erythromycin base:****Tabts:** 250, 500 mg**Delayed-release tabts:** 250, 333, 500 mg**Delayed-release caps:** 250 mg**Topical ointment:** 2% (25 g)**Topical gel:** 2% (30, 60 g); contains alcohol 92%**Topical solution:** 2% (60 mL); may contain 44%–66% alcohol**Topical pad/swab:** 2% (60s)**Ophthalmic ointment:** 0.5% (1, 3.5 g)**Erythromycin ethyl succinate (EES):****Oral suspension:** 200 mg/5 mL (100, 200 mL), 400 mg/5 mL (100 mL)**Oral drops:** 100 mg/2.5 mL (100 mL)**Tabts:** 400 mg**Erythromycin stearate:****Tabts:** 250 mg**Erythromycin lactobionate:****Injection:** 500, 1000 mg; may contain benzyl alcohol**Oral:****Neonate (use EES preparation):**<1.2 kg: 20 mg/kg/24 hr  $\div$  Q12 hr PO $\geq 1.2$  kg:0–7 days: 20 mg/kg/24 hr  $\div$  Q12 hr PO

&gt;7 days:

1.2–2 kg: 30 mg/kg/24 hr  $\div$  Q8 hr PO $\geq 2$  kg: 30–40 mg/kg/24 hr  $\div$  Q6–8 hr PO**Chlamydial conjunctivitis and pneumonia:** 50 mg/kg/24 hr  $\div$  Q6 hr PO  $\times$  14 days; max. dose 2 g/24 hr  
**Child (use base or EES preparation):** 30–50 mg/kg/24 hr  $\div$  Q6–8 hr; max. dose 2 g/24 hr for base preparations and 3.2 g/24 hr for EES preparations**Pertussis:** 40–50 mg/kg/24 hr  $\div$  Q6 hr PO  $\times$  14 days (max. dose 2 g/24 hr); use azithromycin for infants <1 mo old.

ERYTHROMYCIN PREPARATIONS *continued*

**Adult:** 1–4 g/24 hr ÷ Q6 hr; **max. dose** 4 g/24 hr

**Parenteral:**

**Child:** 20–50 mg/kg/24 hr ÷ Q6 hr IV

**Adult:** 15–20 mg/kg/24 hr ÷ Q6 hr IV

**Max. dose:** 4 g/24 hr

**Rheumatic fever prophylaxis:** 500 mg/24 hr ÷ Q12 hr PO

**Ophthalmic:** Apply 0.5-inch ribbon to affected eye BID–QID. Apply as a one-time dose for prophylaxis of neonatal gonococcal ophthalmia.

**Preoperative bowel preparation:** 20 mg/kg/dose PO erythromycin base × 3 doses, with neomycin, 1 day before surgery

**Prokinetic agent:**

**Infant and child:** 10–20 mg/kg/24 hr PO ÷ TID–QID (QAC or QAC and QHS)



**Avoid** use in patients with known QT prolongation, proarrhythmic conditions (e.g., hypokalemia, hypomagnesemia, significant bradycardia), and receiving class IA or class III antiarrhythmic agents, astemizole, cisapride, pimozide, or terfenadine. Hypertrophic pyloric stenosis in neonates receiving prophylactic therapy for pertussis, life-threatening episodes of ventricular tachycardia associated with prolonged QTc interval, and exacerbation of myasthenia gravis have been reported. May produce false-positive urinary catecholamines, 17-hydroxycorticosteroids, and 17-ketosteroids.

GI side effects common (nausea, vomiting, abdominal cramps). Cardiac dysrhythmia, anaphylaxis, interstitial nephritis, and hearing loss have been reported. **Use with caution** in liver disease.

Estolate may cause cholestatic jaundice, although hepatotoxicity is uncommon (2% of reported cases). Inhibits CYP 450 1A2, 3A3/4 isoenzymes. May produce elevated digoxin, theophylline, carbamazepine, clozapine, cyclosporine, and methylprednisolone levels. Adjust dose in renal failure (see Chapter 31). Use ideal body weight for obese patients when calculating doses.

Oral therapy should replace IV as soon as possible. Give oral doses after meals. Because of different absorption characteristics, higher oral doses of EES are needed to achieve therapeutic effects. **Avoid** IM route (pain, necrosis). For ophthalmic use, avoid ointment tip contact with eye or skin.

## ERYTHROPOIETIN

See Epoetin Alfa

## ESMOLOL HCL

Brevibloc and generics

***β<sub>1</sub>-Adrenergic (selective) blocking agent, antihypertensive agent, class II antiarrhythmic***



No



No



?



C

**Injection:** 10 mg/mL (10 mL)

**Injection, premixed infusion in iso-osmotic sodium chloride:** 10 mg/mL (250 mL), 20 mg/mL (100 mL)

**Postoperative hypertension:** Titrate to response (limited information):

**Loading dose:** 500 mcg/kg IV over 1 min

**Maintenance dose:** 50–250 mcg/kg/min IV as infusion. Titrate doses upward 50–100 mcg/kg/min Q5–10 min as needed. Dosages as high as 1000 mcg/kg/min have been administered to children 1–12 yr.

**SVT:** Titrate to response (limited information).

**Loading dose:** 100–500 mcg/kg IV over 1 min

**Maintenance dose:** 25–100 mcg/kg/min IV as infusion. Titrate doses upward 50–100 mcg/kg/min Q5–10 min as needed. Dosages as high as 1000 mcg/kg/min have been administered.



*Continued*

ESMOLOL HCL *continued*

**Contraindicated** in sinus bradycardia, >first-degree heart block, and cardiogenic shock or heart failure. Short duration of action;  $T_{1/2} = 2.9\text{--}4.7$  min for children and 9 min for adults.

May cause bronchospasm, congestive heart failure, hypotension (at doses  $>200$  mcg/kg/min), nausea, and vomiting. May increase digoxin (by 10%–20%) and theophylline levels.

Morphine may increase esmolol level by 46%. Theophylline may decrease esmolol's effects.

**Administer only in a monitored setting.** Concentration for administration is typically  $\leq 10$  mg/mL, but 20 mg/mL has been administered in pediatric patients.

**ESOMEPRAZOLE**

Nexium and other

**Gastric acid proton pump inhibitor**



Yes



No



2



B/C

**Caps, delayed-release:** 20, 40 mg; contains magnesium (NOTE: Another delayed-release capsule product containing strontium may also be available.)

**Powder for oral suspension:** 2.5, 5, 10, 20, 40 mg packets (30s); contains magnesium

**Injection:** 20, 40 mg; contains EDTA

**Child (PO):**

**GERD (use for up to 8 weeks):**

1–11 yr: 10 mg once daily

$\geq 12$  yr: 20–40 mg once daily

**Erosive esophagitis in GERD (use up to 6 weeks):**

**Infant (1 mo–<1 yr):**

3–5 kg: 2.5 mg once daily

$>5\text{--}7.5$  kg: 5 mg once daily

$>7.5\text{--}12$  kg: 10 mg once daily

1–11 yr:

$<20$  kg: 10 mg once daily

$\geq 20$  kg: 10 or 20 mg once daily

**Child (IV):**

**GERD with erosive esophagitis:**

**Infant:** 0.5–1 mg/kg/dose once daily

**Child 1–17 yr:**

$<55$  kg: 10 mg once daily

$\geq 55$  kg: 20–40 mg once daily

**Adult (PO/IV):**

**GERD:** 20 or 40 mg once daily  $\times$  4–8 wk

**Prevention of NSAID-induced gastric ulcers:** 20 or 40 mg once daily for up to 6 mo

**Pathologic hypersecretory conditions (e.g., Zollinger-Ellison syndrome):** 40 mg BID; doses up to 240 mg/24 hr have been used.

**Hepatic impairment:** Patients with severe hepatic function impairment (Child-Pugh class C) should not exceed 20 mg/24 hr.

Cross-allergic reactions with other proton-pump inhibitors (e.g., lansoprazole, pantoprazole, rabeprazole). **Use with caution** in liver impairment (see dosage adjustment recommendation in dosing section). GI disturbances and headache are common. Hypomagnesemia may occur with continuous use. Erythema multiforme, Stevens-Johnson syndrome, TEN, pancreatitis, and fractures of the hip, wrist, and spine (in adults  $>50$  yr old receiving high doses or prolonged therapy  $>1$  yr) have been reported. Drug is a substrate and inhibitor of CYP 450 2C19 and substrate of CYP 450 3A4. May decrease absorption or effects of atazanavir, clopidogrel, ketoconazole, itraconazole, and iron salts. May increase effect/toxicity of diazepam, midazolam, digoxin, carbamazepine, and warfarin. Voriconazole may increase



ESOMEPRAZOLE *continued*

effects of esomeprazole. May be used in combination with clarithromycin and amoxicillin for *Helicobacter pylori* infections.

Pregnancy category is a "B" for the magnesium-containing product and a "C" for the strontium-containing product.

Administer all oral doses before meals and 30 min before sucralfate (if receiving). **Do not** crush or chew capsules. IV doses may be given as fast as 3 min or infused over 10–30 min.

**ETANERCEPT**

Enbrel

**Antirheumatic, immunomodulatory agent, tumor necrosis factor receptor p75 Fc fusion protein**



No



No



3



B

**Prefilled injection:** 25 mg (0.51 mL of 50 mg/mL solution), 50 mg (0.98 mL of 50 mg/mL solution); contains sucrose, L-arginine

**Injection (powder):** 25 mg with diluent (1 mL bacteriostatic water containing 0.9% benzyl alcohol); contains mannitol, sucrose, tromethamine

**Juvenile idiopathic arthritis:**

**Child 2–17 yr:** 0.4 mg/kg/dose SC twice weekly administered 72–96 hr apart; **max. dose** 25 mg. Alternative once-weekly dose of 0.8 mg/kg/dose SC (**max. dose** 50 mg/wk and **max. single injection site dose** of 25 mg) may be used.

**Rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis:**

**Adult:** 25 mg SC twice weekly administered 72–96 hr apart. Alternative once-weekly dose of 50 mg SC (**max. single injection site dose** of 25 mg) may be used.

**Plaque psoriasis:**

**Child and adolescent (4–17 yr; limited data):** 0.8 mg/kg/dose (max. dose 50 mg) SC once weekly

**Adult:** Start with 50 mg SC twice weekly administered 72–96 hr apart  $\times$  3 mo, followed by a reduced maintenance dose of 50 mg SC per wk. Starting doses of 25 mg or 50 mg per wk have also been shown to be effective.

**Max. single injection site dose:** 25 mg

**Contraindicated** in serious infections, sepsis, or hypersensitivity to any of medication

components. **Use with caution** in patients with history of recurrent infections or underlying conditions that may predispose them to infections (including concomitant immunosuppressive therapy), CNS demyelinating disorders, malignancies, immune-related diseases, and latex allergy. Common adverse effects in children include headache, abdominal pain, vomiting, and nausea. Injection site reactions (e.g., discomfort, itching, swelling), rhinitis, dizziness, rash, depression, infections (varicella, aseptic meningitis, rare cases of TB, and fatal/serious infections and sepsis), bone marrow suppression (e.g., aplastic anemia), vertigo, and CNS demyelinating disorder have also been reported. Malignancies (some fatal, and  $\approx$  50% were lymphomas) have been reported in children and adolescents.

**Do not** administer live vaccines concurrently with this drug. In JRA, it is recommended that before initiating therapy, the patient be brought up to date with all immunizations in agreement with current immunization guidelines.

Onset of action is 1–4 wk, with peak effects usually within 3 mo.

Patients must be properly instructed on preparing and administering the medication. Drug requires reconstitution by gently swirling its contents with the supplied diluent (**do not** shake or vigorously agitate) because some foaming will occur. Reconstituted solutions should be clear and colorless and used within 6 hr.

Drug is administered subcutaneously by rotating injection sites (thigh, abdomen, or upper arm) with a **max. single injection site dose** of 25 mg. Administer new injections  $\geq$ 1 inch from an old site and never where the skin is tender, bruised, red, or hard.



**ETHAMBUTOL HCL**

Myambutol and generics

**Antituberculosis drug**

No



Yes



2



C

Tabs: 100, 400 mg

**Tuberculosis:**

**Infant, child, adolescent, and adult:** 15–25 mg/kg/dose PO once daily or  
50 mg/kg/dose PO twice weekly; **max. dose** 2.5 g/24 hr.

***Nontuberculous mycobacterial infection and Mycobacterium avium complex in AIDS (recurrence prophylaxis or treatment; use in combination with other medications):***

**Infant, child, adolescent, and adult:** 15–25 mg/kg/24 hr PO once daily; **max. dose** 2.5 g/24 hr

May cause reversible optic neuritis, especially with larger doses. Obtain baseline ophthalmologic studies before beginning therapy and then monthly. Follow visual acuity, visual fields, and (red-green) color vision. **Do not use** in optic neuritis and in children whose visual acuity cannot be assessed. **Discontinue** if any visual deterioration occurs. Monitor uric acid, liver function, heme status, and renal function. Hyperuricemia, GI disturbances, and mania are common. Erythema multiforme has been reported. Coadministration with aluminum hydroxide can reduce ethambutol's absorption; space administration by 4 hr. Give with food. **Adjust dose with renal failure (see Chapter 31).**

**ETHOSUXIMIDE**

Zarontin and generics

**Anticonvulsant**

Yes



Yes



2



D

Caps: 250 mg

Syrup: 250 mg/5 mL (473 mL)

**Oral:****≤6 yr:**

**Initial:** 15 mg/kg/24 hr ÷ BID; **max. dose** 500 mg/24 hr; increase as needed Q4–7 days.

**Usual maintenance dose:** 15–40 mg/kg/24 hr ÷ BID

**>6 yr and adult:** 250 mg BID; increase by 250 mg/24 hr as needed Q4–7 days.

**Usual maintenance dose:** 20–40 mg/kg/24 hr ÷ BID

**Max. dose (all ages):** 1500 mg/24 hr

**Use with caution** in hepatic and renal disease. Ataxia, anorexia, drowsiness, sleep disturbances, rashes, and blood dyscrasias are rare idiosyncratic reactions. May cause lupus-like syndrome; may increase frequency of grand mal seizures in patients with mixed-type seizures. Serious dermatologic reactions (e.g., Stevens-Johnson syndrome and DRESS) have been reported. May increase risk of suicidal thoughts/behavior. Cases of birth defects have been reported; ethosuximide crosses the placenta. Drug of choice for absence seizures. Carbamazepine, phenytoin, primidone, phenobarbital, valproic acid, nevirapine, and ritonavir may decrease ethosuximide levels.

Therapeutic levels: 40–100 mg/L.  $T_{1/2}$  = 24–42 hr. Recommended serum sampling time at steady state: obtain trough level within 30 min before next scheduled dose after 5–10 days of continuous dosing.

To minimize GI distress, may administer with food or milk. Abrupt withdrawal of drug may precipitate absence status.

**FAMCICLOVIR**

Famvir and generics

**Antiviral**

Yes



Yes



?



B

**Tabs:** 125, 250, 500 mg**Adult:**

**Herpes zoster:** 500 mg Q8 hr PO  $\times$  7 days; initiate therapy promptly as soon as diagnosis is made (initiation within 48 hr after rash onset is ideal; currently no data for starting treatment >72 hr after rash onset).

**Genital herpes (first episode):** 250 mg Q8 hr PO  $\times$  7–10 days

**Recurrent genital herpes:**

**Immunocompetent:** 1000 mg Q12 hr PO  $\times$  1 day or 125 mg Q12 hr PO  $\times$  5 days; initiate therapy at first sign or symptom. Efficacy has not been established when treatment is initiated >6 hr after onset of symptoms or lesions.

**Immunocompromised:** 500 mg Q8 hr PO  $\times$  7 days.

**Suppression of recurrent genital herpes (immunocompetent):** 250 mg Q12 hr PO up to 1 yr, then reassess for HSV infection recurrence.

**Recurrent herpes labialis:**

**Immunocompetent:** 1500 mg PO  $\times$  1

**Immunocompromised:** 500 mg Q8 hr PO  $\times$  7 days

**Recurrent mucocutaneous herpes in HIV:** 500 mg Q12 hr PO  $\times$  7 days



Drug is converted to its active form (penciclovir). Hepatic impairment may impair/reduce conversion of famciclovir to penciclovir. Better absorption than PO acyclovir.

May cause headache, diarrhea, nausea, and abdominal pain. Serious skin reactions (e.g., TEN and Stevens-Johnson syndrome), angioedema, palpitations, cholestatic jaundice, and abnormal LFTs have been reported. Concomitant use with probenecid and other drugs eliminated by active tubular secretion may result in decreased penciclovir clearance. **Reduce dose in renal impairment (see Chapter 31).**

Safety and efficacy in suppression of recurrent genital herpes have not been established beyond 1 yr.

No efficacy data available for children 1–<12 yr to support its use for genital herpes, recurrent herpes labialis, and varicella. Efficacy has not been established for recurrent herpes labialis for children 12–<18 yr. May be administered with or without food.

**FAMOTIDINE**

Pepcid, Pepcid AC [OTC], Maximum Strength Pepcid AC [OTC],  
Pepcid Complete [OTC], Pepcid RPD, and generics

**Histamine-2-receptor antagonist**

No



Yes



1



B

**Injection:** 10 mg/mL (2, 4, 20, 50 mL); multidose vials contain 0.9% benzyl alcohol

**Premixed injection:** 20 mg/50 mL in iso-osmotic sodium chloride

**Oral suspension:** 40 mg/5 mL (contains parabens) (50 mL)

**Tabs:** 10 [OTC], 20 [OTC], 40 mg

**Disintegrating oral tabs (Pepcid RPD):** 20, 40 mg; contains aspartame

**Chewable tabs (Pepcid Complete and others) [OTC]:** 10 mg famotidine with 800 mg calcium carbonate and 165 mg magnesium hydroxide; may contain aspartame

**Neonate and <3 mo:**

**IV:** 0.25–0.5 mg/kg/dose Q24 hr

**PO:** 0.5–1 mg/kg/dose Q24 hr

**$\geq$ 3 mo–1 yr (GERD):** 0.5 mg/kg/dose PO Q12 hr

Continued

FAMOTIDINE *continued***Child (1–12 yr):****IV:** Initial: 0.6–0.8 mg/kg/24 hr ÷ Q8–12 hr up to a **max.** of 40 mg/24 hr**PO:** Initial: 1–1.2 mg/kg/24 hr ÷ Q8–12 hr up to a **max.** of 40 mg/24 hr**Peptic ulcer:** 0.5 mg/kg/24 hr PO QHS or ÷ Q12 hr up to a **max. dose** of 40 mg/24 hr**GERD:** 1–2 mg/kg/24 hr PO ÷ Q12 hr up to a **max. dose** of 80 mg/24 hr**Adolescent and adult:****Duodenal ulcer:****PO:** 20 mg BID or 40 mg QHS × 4–8 wk, then maintenance therapy at 20 mg QHS**IV:** 20 mg BID**GERD:** 20 mg BID PO × 6 wk**Esophagitis:** 20–40 mg BID PO × 12 wk

A Q12-hr dosage interval is generally recommended, but infants and young children may require a Q8-hr interval because of enhanced drug clearance. Headaches, dizziness, constipation, diarrhea, and drowsiness have occurred. **Dosage adjustment is required in severe renal failure (see Chapter 31);** prolonged QT interval has been reported very rarely in patients with renal impairment whose dosage had not been adjusted appropriately.

Shake oral suspension well before each use. Disintegrating oral tablets should be placed on the tongue to be disintegrated and subsequently swallowed. Doses may be administered with or without food.

**FELBAMATE**

Felbatol and generics

**Anticonvulsant**

Yes



Yes



?



C

**Tabs:** 400, 600 mg**Oral suspension:** 600 mg/5 mL**Lennox-Gastaut for child 2–14 yr (adjunctive therapy):**

Start at 15 mg/kg/24 hr PO ÷ TID–QID; increase dosage by 15 mg/kg/24-hr increments at weekly intervals up to a **max. dose** of 45 mg/kg/24 hr or 3600 mg/24 hr (whichever is less). See remarks for adjusting concurrent anticonvulsants.

**Child ≥ 14 yr–adult:**

**Adjunctive therapy:** Start at 1200 mg/24 hr PO ÷ TID–QID; increase dosage by 1200 mg/24 hr at weekly intervals up to a **max. dose** of 3600 mg/day. See remarks for adjusting concurrent anticonvulsants.

**Monotherapy (as initial therapy):** Start at 1200 mg/24 hr PO ÷ TID–QID. Increase dose under close clinical supervision at 600-mg increments Q2 wk to 2400 mg/24 hr. **Max. dose:** 3600 mg/24 hr.

**Conversion to monotherapy:** Start at 1200 mg/24 hr ÷ PO TID–QID for 2 wk, then increase to 2400 mg/24 hr for 1 wk. At wk 3, increase to 3600 mg/24 hr. Reduce dose of other anticonvulsants by 33% at initiation of felbamate, and continue to reduce other anticonvulsants as clinically indicated at wk 2 when felbamate dose is increased.

Drug should be prescribed under strict supervision by a specialist. **Contraindicated** in blood dyscrasias or hepatic dysfunction (prior or current) and hypersensitivity to meprobamate. Aplastic anemia and hepatic failure leading to death have been associated with drug. May cause headache, fatigue, anxiety, GI disturbances, gingival hyperplasia, increased liver enzymes, and bone marrow suppression. Suicidal behavior or ideation have been reported. **Obtain serum levels of concurrent anticonvulsants.** Monitor liver enzymes, bilirubin, CBC with differential, platelets at baseline and Q1–2 wk. Doses should be decreased by 50% in renally impaired patients.



FELBAMATE *continued*

When initiating adjunctive therapy (all ages), doses of other antiepileptic drugs (AEDs) are reduced by 20% to control plasma levels of concurrent phenytoin, valproic acid, phenobarbital, and carbamazepine. Further reductions of concomitant AED dosage may be necessary to minimize side effects caused by drug interactions.

When converting to monotherapy, reduce other AEDs by one third at start of felbamate therapy. Then after 2 wk and at the start of increasing the felbamate dosage, reduce other AEDs by an additional one third. At wk 3, continue to reduce other AEDs as clinically indicated.

Carbamazepine levels may be decreased, whereas phenytoin and valproic acid levels may be increased. Phenytoin and carbamazepine may increase felbamate clearance; valproic acid may decrease its clearance.

Doses can be administered with or without food.

**FENTANYL**

Sublimaze, Duragesic, Fentora, Abstral, Actiq, Lazanda, and many generics

**Narcotic; analgesic, sedative**



No



Yes



2



C/D

**Injection:** 50 mcg/mL

**SR patch (Duragesic and others):** 12.5, 25, 50, 75, 100 mcg/hr (5s)

**Tablets for buccal administration:**

Fentora: 100, 200, 400, 600, 800 mcg (28s)

**Lozenge on a stick:**

Actiq and others: 200, 400, 600, 800, 1200, 1600 mcg (30s)

**Nasal solution:**

Lazanda: 100 mcg/spray, 400 mcg/spray (5 mL; delivers 8 sprays)

**Titrate dose to effect.**

**Neonate and younger infant:**

**Sedation/analgesia:** 1–4 mcg/kg/dose IV Q2–4 hr PRN

**Continuous IV infusion:** 1–5 mcg/kg/hr; tolerance may develop

**Older infant and child:**

**Sedation/analgesia:** 1–2 mcg/kg/dose IV/IM Q30–60 min PRN

**Continuous IV infusion:** 1 mcg/kg/hr; titrate to effect; usual infusion range 1–3 mcg/kg/hr

**To prepare infusion,** use the following formula:

$$50 \times \frac{\text{Desired dose (mcg/kg/hr)}}{\text{Desired infusion rate (mL/hr)}} \times \text{Wt (kg)} = \frac{\text{mcg Fentanyl}}{50 \text{ mL fluid}}$$

**Oral, breakthrough cancer pain for opioid-intolerant patients (see remarks):**

**Buccal tabs (Fentora; ≥18 yr):** Start with 100 mcg by placing tablet in the buccal cavity (above a rear molar, between upper cheek and gum) and letting tablet dissolve for 15–25 min. A second 100 mcg dose, if needed, may be administered 30 min after the start of first dose. If needed, increase dose initially in multiples of 100-mcg tablet when patients require >1 dose per breakthrough pain episode for several consecutive episodes. If titration requires >400 mcg/dose, use 200-mcg tabs.

**Lozenges (≥16 yr):** Start with 200 mcg by placing lozenge in the mouth between cheek and lower gum. If needed, may repeat dose 15 min after the completion of first dose (30 min after start of prior dose). If therapy requires >1 lozenge per episode, consider increasing dose to the next higher strength. Do not give more than 2 doses for each episode of breakthrough pain, and reevaluate long-acting opioid therapy if patient requires >4 doses/24 hr.

*Continued*



FENTANYL *continued*

**Transdermal (see remarks):** Safety has not been established in children <2 yr and should be administered in children ≥2 yr who are opioid tolerant. Use is **contraindicated** in acute or postoperative pain in opiate-naïve patients.

**Opioid-tolerant child receiving at least 60 mg morphine equivalents/24 hr:** Use 25 mcg/hr patch Q72 hr. Patch titration should not occur before 3 days of administration of initial dose or more frequently than Q6 days thereafter.

See Chapter 6 for equianalgesic dosing and PCA dosing.

**Intranasal route for acute and preprocedure analgesia (see remarks):**

≥1 yr–adolescent: 1–2 mcg/kg/dose intranasally (**max. dose** 50 mcg) Q1 hr PRN

**Use with caution** in bradycardia, respiratory depression, and increased intracranial pressure.

**Adjust dose in renal failure (see Chapter 31).** Fatalities and life-threatening respiratory depression have been reported with inappropriate use (overdoses, use in opioid-naïve patients, changing patch too frequently and exposing patch to a heat source) of the transdermal route.

Highly lipophilic and may deposit into fat tissue. IV onset of action 1–2 min, with peak effects in 10 min. IV duration of action 30–60 min. Give IV dose over 3–5 min. Rapid infusion may cause respiratory depression and chest wall rigidity. Respiratory depression may persist beyond the period of analgesia. Transdermal onset of action 6–8 hr, with a 72-hr duration of action. See Chapter 6 for pharmacodynamic information with transmucosal and transdermal routes.

Buccal tabs and oral lozenges are indicated only for management of breakthrough cancer pain in patients already receiving and tolerant to opioid therapy. Buccal tabs (Fentora) and lozenge (Actiq) dosage forms are available through a restricted distribution program (REMS) and are **NOT** bioequivalent (see package insert for conversion).

Intranasal route of administration for analgesia has an onset of action at 10–30 min. Pediatric studies have demonstrated that intranasal fentanyl is equivalent to and better than morphine (PO/IV/IM) and equivalent to IV fentanyl for providing analgesia.

Fentanyl is a substrate for the CYP 450 3A4 enzyme. Be aware of medications that inhibit or induce this enzyme, for it may increase or decrease the effects of fentanyl, respectively.

Pregnancy category changes to “D” if drug is used for prolonged periods or in high doses at term.



## FERRIC GLUCONATE

See Iron – Injectable Preparations

## FERROUS SULFATE

See Iron – Oral Preparations

## FEXOFENADINE ± PSEUDOEPHEDRINE

Allegra, Allegra ODT, Allegra-D 12 Hour, Allegra-D 24 Hour, and generics

**Antihistamine, less-sedating ± decongestant**



No



Yes



2



C

**Tab:** 30, 60, 180 mg

**Tab, orally disintegrating** (Allegra Allergy Childrens; ODT): 30 mg; contains phenylalanine

**Oral suspension:** 6 mg/mL (120 mL)

**Extended-release tab in combination with pseudoephedrine (PE):**

Allegra-D 12 Hour: 60 mg fexofenadine + 120 mg pseudoephedrine

Allegra-D 24 Hour: 180 mg fexofenadine + 240 mg pseudoephedrine

FEXOFENADINE ± PSEUDOEPHEDRINE *continued***Fexofenadine:**

6 mo–&lt;2 yr: 15 mg PO BID

2–11 yr: 30 mg PO BID

≥12 yr–adult: 60 mg PO BID; 180 mg PO once daily may be used in seasonal rhinitis.

**Extended-release tabs of fexofenadine and pseudoephedrine:**

≥12 yr–adult:

**Allegra-D 12 Hour:** 1 tablet PO BID**Allegra-D 24 Hour:** 1 tablet PO once daily

May cause drowsiness, fatigue, headache, dyspepsia, nausea, and dysmenorrhea. Has **not** been implicated in causing cardiac arrhythmias when used with other drugs that are metabolized by hepatic microsomal enzymes (e.g., ketoconazole, erythromycin). **Reduce dose to 30 mg PO once daily for child 6–11 yr old and 60 mg PO once daily for ≥12 yr old if CrCl < 40 mL/min.** For use of Allegra-D 12 Hour and decreased renal function, an initial dose of 1 tablet PO once daily is recommended. Avoid use of Allegra-D 24 Hour in renal impairment. See *Pseudoephedrine* for additional remarks if using the combination product.

Medication as the single agent may be administered with or without food. **Do not** administer antacids with or within 2 hr of fexofenadine dose. The extended-release combination product should be swallowed whole without food.

**FILGRASTIM**

Neupogen, G-CSF

**Colony-stimulating factor**

No



No



?



C

**Injection:** 300 mcg/mL (1, 1.6 mL vials)

Injection, prefilled syringes with 27-gauge, ½-inch needles: 600 mcg/mL (300 mcg per 0.5 mL and 480 mcg per 0.8 mL) (10s)

**All dosage forms are preservative free.****Individual protocols may direct dosing.****IV/SC:** 5–10 mcg/kg/dose once daily × 14 days or until ANC > 10,000/mm<sup>3</sup>. Dosage may be increased by 5 mcg/kg/24 hr if desired effect is not achieved within 7 days.Discontinue therapy when ANC > 10,000/mm<sup>3</sup>.

May cause bone pain, fever, and rash. Monitor CBC, uric acid, and LFTs. Thrombocytopenia and decreased bone density/osteoporosis in pediatric patients with severe chronic neutropenia have been reported. **Use with caution** in patients with malignancies with myeloid characteristics. **Contraindicated** for patients sensitive to *Escherichia coli*-derived proteins.

**Do not** administer 24 hr before or after administration of chemotherapy.

SC routes of administration are preferred because of prolonged serum levels over IV route. If used via IV route and G-CSF final concentration < 15 mcg/mL, add 2 mg albumin/1 mL of IV fluid to prevent drug adsorption to the IV administration set.

**FLECAINIDE ACETATE**

Tambacor and generics

**Antiarrhythmic, class Ic**

Yes



Yes



2



C

**Tabs:** 50, 100, 150 mg**Oral suspension:** 5, 20 mg/mL 

**Child:** Initial: 1–3 mg/kg/24 hr ÷ Q8 hr PO; usual range: 3–6 mg/kg/24 hr ÷ Q8 hr PO. Monitor serum levels to adjust dose if needed.

*Continued*

FLECAINIDE ACETATE *continued***Adult:**

**Sustained V tach:** 100 mg PO Q12 hr; may increase by 50 mg Q12 hr (100 mg/24 hr) Q4 days to **max. dose** of 600 mg/24 hr.

**Paroxysmal SVT/paroxysmal AF:** 50 mg PO Q12 hr; may increase dose by 50 mg Q12 hr Q4 days to **max. dose** of 300 mg/24 hr.

May aggravate LV failure, sinus bradycardia, preexisting ventricular arrhythmias. May cause AV block, dizziness, blurred vision, dyspnea, nausea, headache, and increased PR or QRS intervals.

**Reserve for life-threatening cases. Use with caution** in renal and/or hepatic impairment.

Flecainide is a substrate for the CYP 450 2D6 enzyme. Be aware of medications that inhibit (e.g., certain SSRIs) or induce this enzyme, for it may increase or decrease effects of flecainide, respectively.

Therapeutic trough level: 0.2–1 mg/L. Recommended serum sampling time at steady state: Obtain trough level within 30 min before next scheduled dose after 2–3 days of continuous dosing for children; after 3–5 days for adults. **Adjust dose in renal failure (see Chapter 31).**

**FLUCONAZOLE**

Diflucan and generics

**Antifungal agent**



Yes



Yes



2



C/D

**Tabs:** 50, 100, 150, 200 mg

**Injection:** 2 mg/mL (50, 100, 200 mL); contains 9 mEq Na/2 mg drug

**Oral suspension:** 10 mg/mL (35 mL), 40 mg/mL (35 mL)

**Neonate (IV/PO):**

**Loading dose:** 12–25 mg/kg

**Maintenance dose:** 6–12 mg/kg, with the following dosing intervals (see table); use higher doses for severe infections of *Candida* strains with MICs >4–8 mcg/mL.



Postconceptional Age (wk)	Postnatal Age (days)	Dosing Interval (hr) & Time (hr) to Start First Maintenance Dose after Load
≤29	0–14	48
	>14	24
≥30	0–7	48
	>7	24

**Child (IV/PO):**

Indication	Loading Dose	Maintenance Dose (Q24 hr) to Begin 24 hr after Loading Dose
Oropharyngeal candidiasis	6 mg/kg	3 mg/kg
Esophageal candidiasis	12 mg/kg	6 mg/kg
Invasive systemic candidiasis and cryptococcal meningitis	12 mg/kg	6–12 mg/kg
Suppressive therapy for HIV infected with cryptococcal meningitis	6 mg/kg	6 mg/kg

**Max. dose:** 12 mg/kg/24 hr

**Adult:**

**Oropharyngeal and esophageal candidiasis:** Loading dose of 200 mg PO/IV, followed by 100 mg Q24 hr (24 hr after load); doses up to **max. dose** of 400 mg/24 hr should be used for esophageal candidiasis.

**Systemic candidiasis and cryptococcal meningitis:** Loading dose of 400 mg PO/IV, followed by 200–800 mg Q24 hr (24 hr after load).

**Bone marrow transplant prophylaxis:** 400 mg PO/IV Q24 hr

FLUCONAZOLE *continued***Suppressive therapy, HIV infected, and cryptococcal meningitis:** 200 mg PO/IV Q24 hr**Vaginal candidiasis:** 150 mg PO  $\times$  1Cardiac arrhythmias may occur when used with cisapride; concomitant use is **contraindicated**.May cause nausea, headache, rash, vomiting, abdominal pain, hepatitis, cholestasis, and diarrhea. Neutropenia, agranulocytosis, and thrombocytopenia have been reported. **Use with caution** in hepatic or renal dysfunction and in patients with proarrhythmic conditions.

Inhibits CYP 450 2C9/10 and CYP 450 3A3/4 (weak inhibitor). May increase effects, toxicity, or levels of cyclosporine, midazolam, phenytoin, rifabutin, tacrolimus, theophylline, warfarin, oral hypoglycemics, and AZT. Rifampin increases fluconazole metabolism.

Pediatric to adult dose equivalency: Every 3 mg/kg-pediatric dosage is equal to 100-mg adult dosage.

Consider using higher doses in morbidly obese patients. **Adjust dose in renal failure (see Chapter 31).**

Pregnancy category is "C" for single 150-mg use for vaginal candidiasis; category "D" for all other indications (high-dose use during first trimester of pregnancy may result in birth defects).

**FLUCYTOSINE**

Ancobon, 5-FC, 5-Fluorocytosine, and generics

**Antifungal agent****Caps:** 250, 500 mg**Oral liquid:** 10 mg/mL**Neonate:** 80–160 mg/kg/24 hr  $\div$  Q6 hr PO**Child and adult:** 50–150 mg/kg/24 hr  $\div$  Q6 hr POMonitor CBC, BUN, serum creatinine, alkaline phosphatase, AST, and ALT. Common side effects: nausea, vomiting, diarrhea, rash, CNS disturbance, anemia, leukopenia, and thrombocytopenia. Use is **contraindicated** in the first trimester of pregnancy.

Therapeutic levels: 25–100 mg/L. Recommended serum sampling time at steady state: Obtain peak level 2–4 hr after oral dose, after 4 days of continuous dosing. Peak levels of 40–60 mg/L have been recommended for systemic candidiasis. Maintain trough levels above 25 mg/L. Prolonged levels above 100 mg/L can increase risk for bone marrow suppression. Bone marrow suppression in immunosuppressed patients can be irreversible and fatal.

Flucytosine interferes with creatinine assay tests using the dry-slide enzymatic method (Kodak Ektachem analyzer). **Adjust dose in renal failure (see Chapter 31).****FLUDROCORTISONE ACETATE**

Florinef acetate, 9-Fluorohydrocortisone, Fluohydrisone, and various generics

**Corticosteroid****Tabs:** 0.1 mg**Infant and child:** 0.05–0.1 mg/24 hr once daily PO**Congenital adrenal hyperplasia:** 0.05–0.3 mg/24 hr once daily PO**Adult:** 0.05–0.2 mg/24 hr once daily PO**Contraindicated** in CHF and systemic fungal infections. Has primarily mineralocorticoid activity. **Use with caution** in hypertension, edema, or renal dysfunction. May cause hypertension, hypokalemia, acne, rash, bruising, headaches, GI ulcers, and growth suppression.

Monitor BP and serum electrolytes. See Chapter 10 for steroid potency comparison.

*Continued*

FLUDROCORTISONE ACETATE *continued*

Drug interactions: Drug's hypokalemic effects may induce digoxin toxicity; phenytoin and rifampin may increase fludrocortisone metabolism.

Doses 0.2–2 mg/24 hr have been used in the management of severe orthostatic hypotension in adults. Use a gradual dosage taper when discontinuing therapy.

**FLUMAZENIL**

Romazicon and generics

**Benzodiazepine antidote**



Yes



No



?



C

**Injection:** 0.1 mg/mL (5, 10 mL); contains parabens

**Benzodiazepine overdose (IV, see remarks):**

**Child (limited data):** 0.01 mg/kg (**max. dose** 0.2 mg) Q1 min PRN to a **max. total cumulative dose** of 1 mg. As an alternative for repeat bolus doses, a continuous infusion of 0.005–0.01 mg/kg/hr has been used.

**Adult:** Initial dose of 0.2 mg over 30 sec; if needed, give 0.3 mg 30 sec later over 30 sec. Additional doses of 0.5 mg given over 30 sec Q1 min PRN up to a cumulative dose of 3 mg (**usual cumulative dose** 1–3 mg). Patients with only partial response to 3 mg may require additional slow titration to a total of 5 mg.

**Reversal of benzodiazepine sedation (IV):**

**Child:** Initial dose of 0.01 mg/kg (**max. dose** 0.2 mg) given over 15 sec; if needed, after 45 sec, give 0.01 mg/kg (**max. dose** 0.2 mg) Q1 min to a **max. total cumulative dose** of 0.05 mg/kg or 1 mg, whichever is lower. Usual total dose: 0.08–1 mg (average 0.65 mg).

**Adult:** Initial dose of 0.2 mg over 15 sec; if needed after 45 sec, give 0.2 mg Q1 min to a **max. total cumulative dose** of 1 mg. Doses may be repeated at 20-min intervals (**max. dose** of 1 mg per 20-min interval) up to a **max. dose** of 3 mg in 1 hr.

**Does not reverse narcotics.** Onset of benzodiazepine reversal occurs in 1–3 min. Reversal effects of flumazenil ( $T_{1/2} \approx 1$  hr) may wear off sooner than benzodiazepine effects. If patient does not respond after cumulative 1–3 mg dose, suspect agent other than benzodiazepines.



May precipitate seizures, especially in patients taking benzodiazepines for seizure control or in patients with tricyclic antidepressant overdose. Fear and panic attacks in patients with history of panic disorders have been reported.

**Use with caution** in liver dysfunction; flumazenil's clearance is significantly reduced. Use normal dose for initial dose, and decrease dosage and frequency for subsequent doses.

See Chapter 2 for complete management of suspected ingestions.

**FLUNISOLIDE**

Nasal solution: Nasarel and generics

Oral inhaler: Aerospan

**Corticosteroid**



No



No



1



C

**Nasal solution:**

Nasarel and generics: 25 mcg/spray (200 sprays/bottle) (25 mL)

**Oral aerosol inhaler:**

Aerospan: 80 mcg/dose (60 doses/5.1 g, 120 doses/8.9 g); CFC-free (HFA)

FLUNISOLIDE *continued*

*For all dosage forms, after symptoms are controlled, reduce to lowest effective maintenance dose (i.e., 1 spray each nostril once daily) to control symptoms.*

**Nasal solution:****Child (6–14 yr):**

**Initial:** 1 spray per nostril TID or 2 sprays per nostril BID; **max. dose** of 4 sprays per nostril/24 hr  
**≥15 yr and adult:**

**Initial:** 2 sprays per nostril BID; if needed, in 4–7 days, increase to 2 sprays per nostril TID; **max. dose** of 8 sprays per nostril/24 hr

**Oral inhaler (see remarks):****Aerospan:**

**Child 6–11 yr:** 1 puff BID; **max. dose** of 4 puffs/24 hr

**Adult:** 2 puffs BID; **max. dose** of 8 puffs/24 hr

May cause a reduction in growth velocity. Shake inhaler or nasal solution well before use. Patients using nasal solution should clear nasal passages before use.



**Do not use** a spacer with Aerospan; product has a self-contained spacer. To prevent thrush, patient/parent should be instructed to rinse mouth after administering drug by inhaler.

**FLUORIDE**

Luride, Fluoritab, Pediaflor, and many others

**Mineral**

No



No



?



B

**Concentrations and strengths based on fluoride ion:**

**Oral drops:** 0.125 mg/drop (30 mL), 0.25 mg/drop (24 mL), 0.5 mg/mL (50 mL)

**Oral solution (rinse):** 0.2, 2 mg/mL

**Chewable tabs:** 0.25, 0.5, 1 mg

**Lozenges:** 1 mg

See Chapter 21 for fluoride-containing multivitamins.

**All doses/24 hr (see table below):**

Recommendations from American Academy of Pediatrics and American Dental Association.



Age	Concentration of Fluoride in Drinking Water (ppm)		
	<0.3	0.3–0.6	>0.6
Birth–6 mo	0	0	0
6 mo–3 yr	0.25 mg	0	0
3–6 yr	0.5 mg	0.25 mg	0
6–16 yr	1 mg	0.5 mg	0

**Contraindicated** in areas where drinking water fluoridation is >0.7 ppm. **Acute overdose:** GI distress, salivation, CNS irritability, tetany, seizures, hypocalcemia, hypoglycemia, cardiorespiratory failure. Chronic excess use may result in mottled teeth or bone changes. Take with food, but **not** milk, to minimize GI upset. The doses have been decreased owing to concerns over dental fluorosis.



**FLUOXETINE HYDROCHLORIDE**

Prozac, Sarafem, Prozac Weekly, and various generics  
*Antidepressant, selective serotonin reuptake inhibitor*



Yes



Yes



X



C

**Oral solution:** 20 mg/5 mL; may contain alcohol

**Caps:** 10, 20, 40 mg

**Delayed-released caps (Prozac Weekly):** 90 mg

**Tabs:** 10, 20, 60 mg

**Depression:**

**Child, 8–18 yr:** Start at 10–20 mg once daily PO. If started on 10 mg/24 hr, may increase dose to 20 mg/24 hr after 1 wk. Use lower 10-mg/24 hr initial dose for lower-weight children; if needed, increase to 20 mg/24 hr after several weeks.

**Adult:** Start at 20 mg once daily PO. May increase after several wk by 20-mg/24-hr increments to **max. dose** of 80 mg/24 hr. Doses >20 mg/24 hr should be divided BID.

**Obsessive-compulsive disorder:**

**Child, 7–18 yr:**

**Lower-weight child:** Start at 10 mg once daily PO. May increase after several wk. Usual dose range: 20–30 mg/24 hr. There is very minimal experience with doses >20 mg/24 hr and no experience with doses >60 mg/24 hr.

**Higher-weight child and adolescent:** Start at 10 mg once daily PO and increase dose to 20 mg/24 hr after 2 wk. May further increase dose after several wk. Usual dose range: 20–60 mg/24 hr.

**Bulimia:**

**Adolescent (PO; limited data):** 20 mg QAM  $\times$  3 days, then 40 mg QAM  $\times$  3 days, then 60 mg QAM.

**Adult:** 60 mg QAM PO; it is recommended to titrate up to this dose over several days.

**Premenstrual dysphoric disorder:**

**Adult:** Start at 20 mg once daily PO using the Sarafem product. **Max. dose:** 80 mg/24 hr. Systematic evaluation has shown that efficacy is maintained for periods of 6 mo at a dose of 20 mg/day. Reassess patients periodically to determine the need for continued treatment.

**Contraindicated** in patients taking MAO inhibitors (e.g., linezolid); possibility of seizures, hyperpyrexia, and coma. **Use with caution** in patients receiving diuretics, or with liver (reduce dose with cirrhosis) or renal impairment. May increase effects of tricyclic antidepressants. May cause headache, insomnia, nervousness, drowsiness, GI disturbance, and weight loss. Increased bleeding diathesis with unaltered prothrombin time may occur with warfarin. Hyponatremia has been reported. Monitor for clinical worsening of depression and suicidal ideation/behavior after initiation of therapy or after dose changes.

May displace other highly protein-bound drugs. Inhibits CYP 450 2C19, 2D6, and 3A3/4 drug metabolism isoenzymes, which may increase effects or toxicity of drugs metabolized by these enzymes. Use with serotonergic drugs (e.g., triptans, methylene blue) and drugs that impair serotonin metabolism (MAOIs) may increase risk for serotonin syndrome. Carefully review patients' medication profile for potential interactions.

Delayed-release capsule is currently indicated for depression and is dosed at 90 mg Q7 days. It is unknown whether weekly dosing provides same protection from relapse as daily dosing.

Breast-feeding is not recommended by the manufacturer; adverse events to nursing infants have been reported. Fluoxetine and metabolite are variable and are higher when compared with other SSRIs. Maternal use of SSRIs during pregnancy and postpartum may result in more difficult breast-feeding. Infants exposed to SSRIs during pregnancy may also have increased risk for persistent pulmonary hypertension of the newborn.

**FLUTICASONE PROPIONATE**

Flonase HFA, Cutivate, Flovent Diskus, Veramyst, and selected generics

**Corticosteroid**

Yes



No



2



C

**Nasal spray:**

**Flonase and generics (as fluticasone propionate):** 50 mcg/actuation (16 g = 120 doses)

**Veramyst (as fluticasone furoate):** 27.5 mcg/actuation (10 g = 120 doses)

**Topical cream (Cutivate and generics):** 0.05% (15, 30, 60 g)

**Topical ointment (Cutivate and generics):** 0.005% (15, 30, 60 g)

**Topical lotion (Cutivate and generics):** 0.05% (60, 120 mL)

**Aerosol inhaler (MDI) (Flovent HFA):** 44 mcg/actuation (10.6 g), 110 mcg/actuation (12 g), 220 mcg/actuation (12 g); each inhaler provides 120 metered inhalations.

**Dry-powder inhalation (DPI) (Flovent Diskus):** 50 mcg/dose, 100 mcg/dose, 250 mcg/dose; all strengths come in a package of 15 Rotadisks; each Rotadisk provides 4 doses, for a total of 60 doses per package.

**Intranasal (allergic rhinitis):****Fluticasone propionate (Flonase and others):**

**≥4 yr and adolescent:** 1 spray (50 mcg) per nostril once daily. Dose may be increased to 2 sprays (100 mcg) per nostril once daily if inadequate response or severe symptoms. Reduce to 1 spray per nostril once daily when symptoms are controlled.

**Adult:** Initial 200 mcg/24 hr (2 sprays [100 mcg]) per nostril once daily; *OR* 1 spray (50 mcg) per nostril BID. Reduce to 1 spray per nostril once daily when symptoms are controlled.

**Max. dose (4 yr–adult):** 2 sprays (100 mcg) per nostril/24 hr

**Fluticasone furoate (Veramyst):**

**2–11 yr:** 1 spray (27.5 mcg) per nostril once daily. If needed, dose may be increased to 2 sprays each nostril once daily. Reduce to 1 spray per nostril once daily when symptoms are controlled.

**≥11 and adult:** 2 sprays (55 mcg) each nostril once daily. Reduce to 1 spray per nostril once daily when symptoms are controlled.

**Max. dose (2 yr–adult):** 2 sprays (55 mcg) per nostril/24 hr

**Oral inhalation (asthma):** Divide all 24-hr doses BID. If desired response is not seen after 2 wk of starting therapy, increase dosage. Then reduce to lowest effective dose when asthma symptoms are controlled. Administration of MDI with aerochamber enhances drug delivery.

**RECOMMENDED DOSAGES FOR ASTHMA**

Age	Previous Use of Bronchodilators Only (max. dose)	Previous Use of Inhaled Corticosteroid (max. dose)	Previous Use of Oral Corticosteroid (max. dose)
Child (4–11 yr)	MDI: 88 mcg/24 hr (176 mcg/24 hr) DPI: 100 mcg/24 hr (200 mcg/24 hr)	MDI: 88 mcg/24 hr (176 mcg/24 hr) DPI: 100 mcg/24 hr (200 mcg/24 hr)	Dose not available
≥12 yr and adult	MDI: 176 mcg/24 hr (880 mcg/24 hr) DPI: 200 mcg/24 hr (1000 mcg/24 hr)	MDI: 176–440 mcg/24 hr (880 mcg/24 hr) DPI: 200–500 mcg/24 hr (1000 mcg/24 hr)	MDI: 880 mcg/24 hr (1760 mcg/24 hr) DPI: 1000–2000 mcg/24 hr (2000 mcg/24 hr)

DPI, Dry-powder inhaler; MDI, metered dose inhaler.

**Eosinophilic esophagitis (limited data; use oral HFA dosage form without spacer for PO administration):**

**Child (1–10 yr):** 220 mcg QID × 4 wk, then 220 mcg TID × 3 wk, then 220 mcg BID × 3 wk, and 220 mcg once daily × 2 wk

Continued



FLUTICASONE PROPIONATE *continued*

**Child ≥ 11 and adolescent:** 440 mcg QID × 4 wk, then 440 mcg TID × 3 wk, then 440 mcg BID × 3 wk, and 440 mcg once daily × 2 wk

**Topical (reassess diagnosis if no improvement in 2 wk):**

**Cream (see Chapter 8 for topical steroid comparisons):**

≥ 3 mo and adult: Apply thin film to affected areas once daily–BID; then reduce to a less potent topical agent when symptoms are controlled.

**Lotion (see remarks):**

≥ 1 yr and adult: Apply thin film to affected areas once daily. Safety of use has not been evaluated longer than 4 wk.

**Ointment:**

**Adult:** Apply thin film to affected areas BID.

Concurrent administration with ritonavir and other CYP 450 3A4 inhibitors may increase fluticasone levels, resulting in Cushing syndrome and adrenal suppression. **Use with caution** and monitor closely in hepatic impairment.



**Intranasal:** Clear nasal passages before use. May cause epistaxis and nasal irritation, which are usually transient. Taste and smell alterations, rare hypersensitivity reactions (angioedema, pruritus, urticaria, wheezing, dyspnea), and nasal septal perforation have been reported in postmarketing studies.

**Oral inhalation:** Rinse mouth after each use. May cause dysphonia, oral thrush, and dermatitis.

Compared with beclomethasone, has been shown to have less of an effect on suppressing linear growth in asthmatic children. Eosinophilic conditions may occur with the withdrawal or decrease of oral corticosteroids after initiation of inhaled fluticasone.

**Topical use:** Avoid application/contact to face, eyes, and open skin. Occlusive dressings are not recommended; they may increase local side effects (irritation, folliculitis, acneiform eruptions, hypopigmentation, perioral dermatitis, contact dermatitis, secondary infection, skin atrophy, striae, hypertrichosis, miliaria). **Do not use** lotion dosage form with formaldehyde hypersensitivity.

**FLUTICASONE PROPIONATE AND SALMETEROL**

Advair Diskus, Advair HFA

**Corticosteroid and long-acting  $\beta_2$ -adrenergic agonist**



Yes



No



2



C

**Dry-powder inhalation (DPI) (Advair Diskus; contains lactose):**

100 mcg fluticasone propionate + 50 mcg salmeterol per inhalation (14, 60 inhalations)

250 mcg fluticasone propionate + 50 mcg salmeterol per inhalation (60 inhalations)

500 mcg fluticasone propionate + 50 mcg salmeterol per inhalation (60 inhalations)

**Aerosol inhaler (MDI) (Advair HFA):**

45 mcg fluticasone propionate + 21 mcg salmeterol per inhalation (8 g delivers 60 doses, 12 g delivers 120 doses)

115 mcg fluticasone propionate + 21 mcg salmeterol per inhalation (8 g delivers 60 doses, 12 g delivers 120 doses)

230 mcg fluticasone propionate + 21 mcg salmeterol per inhalation (8 g delivers 60 doses, 12 g delivers 120 doses)

**Asthma:**

**Without prior inhaled steroid use:**

**Dry-powder inhalation (DPI):**

**4 yr–adult:** Start with one inhalation BID of 100 mcg fluticasone propionate + 50 mcg salmeterol.

**Aerosol inhaler (MDI):**

≥ 12 yr and adult: 2 inhalations BID of 45 mcg fluticasone + 21 mcg salmeterol, *OR* 115 mcg fluticasone + 21 mcg salmeterol; **max. dose** is 2 inhalations BID of 230 mcg fluticasone + 21 mcg salmeterol.



FLUTICASONE PROPIONATE AND SALMETEROL *continued**With prior inhaled steroid use (conversion from other inhaled steroids; see following table):*

Inhaled Corticosteroid	Current Daily Dose	Recommended Strength of Fluticasone Propionate + Salmeterol Diskus (DPI) (Advair Diskus) Administered at 1 Inhalation BID	Recommended Strength of Fluticasone Propionate + Salmeterol Aerosol Inhaler (MDI) (Advair HFA) Administered at 2 Inhalations BID
Beclomethasone dipropionate (Qvar; CFC-free, HFA)	160 mcg 320 mcg 640 mcg	100 mcg + 50 mcg 250 mcg + 50 mcg 500 mcg + 50 mcg	45 mcg + 21 mcg 115 mcg + 21 mcg 230 mcg + 21 mcg
Budesonide	≤400 mcg 800–1200 mcg 1600 mcg	100 mcg + 50 mcg 250 mcg + 50 mcg 500 mcg + 50 mcg	45 mcg + 21 mcg 115 mcg + 21 mcg 230 mcg + 21 mcg
Flunisolide (Aerobid, Aerobid-M; containing CFCs)	≤1000 mcg 1250–2000 mcg	100 mcg + 50 mcg 250 mcg + 50 mcg	45 mcg + 21 mcg 115 mcg + 21 mcg
Flunisolide (Aerospan; CFC-free, HFA)	≤320 mcg 640 mcg	100 mcg + 50 mcg 250 mcg + 50 mcg	45 mcg + 21 mcg 115 mcg + 21 mcg
Fluticasone propionate aerosol (HFA)	≤176 mcg 440 mcg 660–880 mcg	100 mcg + 50 mcg 250 mcg + 50 mcg 500 mcg + 50 mcg	45 mcg + 21 mcg 115 mcg + 21 mcg 230 mcg + 21 mcg
Fluticasone propionate dry powder (DPI)	≤200 mcg 500 mcg 1000 mcg	100 mcg + 50 mcg 250 mcg + 50 mcg 500 mcg + 50 mcg	45 mcg + 21 mcg 115 mcg + 21 mcg 230 mcg + 21 mcg
Mometasone furoate	220 mcg 440 mcg 880 mcg	100 mcg + 50 mcg 250 mcg + 50 mcg 500 mcg + 50 mcg	45 mcg + 21 mcg 115 mcg + 21 mcg 230 mcg + 21 mcg
Triamcinolone	≤1000 mcg 1100–1600 mcg	100 mcg + 50 mcg 250 mcg + 50 mcg	45 mcg + 21 mcg 115 mcg + 21 mcg

**Max. doses:****Dry-powder inhalation (DPI):** 1 inhalation BID of 500 mcg fluticasone propionate + 50 mcg salmeterol**Aerosol inhaler (MDI):** 2 inhalations BID of 230 mcg fluticasone propionate + 21 mcg salmeterol

See *Fluticasone Propionate* and *Salmeterol* for remarks. Titrate to lowest effective strength after asthma is adequately controlled. Proper patient education, including dosage administration technique, is essential. See package insert for detailed instructions. Rinse mouth after each use.

**FLUVOXAMINE**

Luvox CR (previously available as Luvox), many generics

**Antidepressant, selective serotonin reuptake inhibitor**

Yes



No



2



C

**Tabs:** 25, 50, 100 mg**Extended-release capsules (Luvox CR and generics):** 100, 150 mg**Obsessive compulsive disorder (use immediate-release tablets unless noted otherwise):**

**8–17 yr:** Start at 25 mg PO QHS. Dose may be increased by 25 mg/24 hr Q7–14 days (slower titration for minimizing behavioral side effects). Total daily doses >50 mg/24 hr should be divided BID. Female patients may require lower dosages than males.

*Continued*

FLUVOXAMINE *continued*

**Max. dose:** *Child:* 8–11 yr: 200 mg/24 hr; *child* ≥ 12–17 yr: 300 mg/24 hr

**Adult:** Start at 50 mg PO QHS. Dose may be increased by 50 mg/24 hr Q4–7 days up to a **max. dose** of 300 mg/24 hr. Total daily doses >100 mg/24 hr should be divided BID.

**Extended-release capsule (adult):** Start at 100 mg PO QHS. Dose may be increased by 50 mg/24 hr Q7 days up to a **max. dose** of 300 mg/24 hr.

**Contraindicated** with coadministration of cisapride, pimozide, thioridazine, tizanidine, or MAO inhibitors. **Use with caution** in hepatic disease (dosage reduction may be necessary); drug is extensively metabolized by liver. Monitor for clinical worsening of depression and suicidal ideation/behavior after initiation of therapy or after dose changes.

Inhibits CYP 450 1A2, 2C19, 2D6, and 3A3/4, which may increase effects or toxicity of drugs metabolized by these enzymes. Dose-related use of thioridazine with fluvoxamine may cause prolongation of QT interval and serious arrhythmias. May increase warfarin plasma levels by 98% and prolong PT. May increase toxicity and/or levels of theophylline, caffeine, and tricyclic antidepressants. Side effects include headache, insomnia, somnolence, nausea, diarrhea, dyspepsia, and dry mouth.

Titrate to lowest effective dose. Consider benefits vs. potential risk for maternal use in breast-feeding. Maternal use during pregnancy and postpartum may result in breast-feeding difficulties.

**FOLIC ACID**

Folvite and many generics

**Water-soluble vitamin**



No



No




1



A/C

**Tabs (OTC):** 0.4, 0.8, 1 mg

**Caps:** 0.4 mg [OTC], 0.8 mg [OTC], 5 mg, 20 mg

**Oral solution:** 50 mcg/mL 

**Injection:** 5 mg/mL; contains 1.5% benzyl alcohol

For U.S. RDA, see Chapter 21.

**Folic acid deficiency PO, IM, IV, SC (see following table):**

Infant	Child 1–10 yr	Child ≥ 11 yr and Adult
<b>INITIAL DOSE</b>		
15 mcg/kg/dose; max. dose 50 mcg/24 hr	1 mg/dose	1 mg/dose
<b>MAINTENANCE</b>		
30–45 mcg/24 hr once daily	0.1–0.4 mg/24 hr once daily	0.4 mg/24 hr once daily Pregnant/lactating women: 0.8 mg/24 hr once daily

Normal levels: See Chapter 21. May mask hematologic effects of vitamin B<sub>12</sub> deficiency but will not prevent progression of neurologic abnormalities. High-dose folic acid may decrease absorption of phenytoin.

Women of childbearing age considering pregnancy should take at least 0.4 mg once daily before and during pregnancy to reduce risk of neural tube defects in the fetus. Pregnancy category changes to “C” if used in doses above the RDA.

**FOMEPIZOLE**

Antizol and generics

**Antidote for ethylene glycol or methanol toxicity**

No



Yes



?



C

**Injection:** 1 g/ mL (1.5 mL)**Child and adult not requiring hemodialysis (IV, all doses administered over 30 min):****Loading dose:** 15 mg/kg/dose  $\times$  1**Maintenance:** 10 mg/kg/dose Q12 hr  $\times$  4 doses, then 15 mg/kg/dose Q12 hr until ethylene glycol or methanol level decreases to  $<20$  mg/dL and patient is asymptomatic, with normal pH.**Child and adult requiring hemodialysis (IV after recommended doses at intervals indicated here.****Fomepizole is removed by dialysis. All doses administered IV over 30 min):****Dosing at beginning of hemodialysis:****If  $<6$  hr since last fomepizole dose:** **DO NOT** administer dose.**If  $\geq 6$  hr since last fomepizole dose:** Administer next scheduled dose.**Dosing during hemodialysis:** Administer Q4 hr or as continuous infusion of 1–1.5 mg/kg/hr.**Dosing at the time hemodialysis is completed (based on time between last dose and end of hemodialysis):** **$<1$  hr:** **DO NOT** administer dose at end of hemodialysis.**1–3 hr:** Administer half of next scheduled dose. **$>3$  hr:** Administer next scheduled dose.**Maintenance dose off hemodialysis:** Give next scheduled dose 12 hr from last dose administered.

Works by competitively inhibiting alcohol dehydrogenase. Safety and efficacy in pediatrics have not been established. **Contraindicated** in hypersensitivity to any components or other pyrazole compounds. Most frequent side effects include headache, nausea, and dizziness. Fomepizole is extensively eliminated by kidneys (**use with caution** in renal failure) and removed by hemodialysis.

Drug product may solidify at temperatures  $<25^{\circ}\text{C}$  ( $77^{\circ}\text{F}$ ); vial can be liquefied by running it under warm water (efficacy, safety, and stability are not affected). All doses must be diluted with at least 100 mL of D<sub>5</sub>W or NS to prevent vein irritation.

**FORMOTEROL**

Foradil Aerolizer, Perforomist

 **$\beta_2$ -Adrenergic agonist (long-acting)**

No



No



2



C

**Inhalation powder in capsules (Foradil Aerolizer):** 12 mcg (12s and 60s); contains lactose and milk proteins. Use with Aerolizer inhaler**Inhalation solution (Perforomist):** 20 mcg/2 mL (60s) **$\geq 5$  yr and adult:****Asthma/bronchodilation (should be used with an inhaled corticosteroid):****Foradil Aerolizer:** 12 mcg Q12 hr; **max. dose** of 24 mcg/24 hr (12 mcg spaced 12 hr apart)**Prevention of exercise-induced asthma for patients NOT receiving maintenance long-acting  $\beta_2$ -agonists (e.g., formoterol or salmeterol):****Foradil Aerolizer:** 12 mcg 15 min before exercise. If needed, an additional dose may be givenAFTER 12 hr. **Max. dose:** 24 mcg/24 hr (12 mcg spaced 12 hr apart). Consider alternative therapy if maximal dosage is not effective.

Continued

FORMOTEROL *continued*

Fast onset of action (1–3 min), with peak effects in 0.5–1 hr and long duration (up to 12 hr).

Although long-acting  $\beta_2$ -adrenergic agonists may decrease the frequency of asthma episodes, they may make asthma episodes more severe when they occur. **Use with caution** in seizures, thyrotoxicosis, diabetes, ketoacidosis, aneurysm, and pheochromocytoma.

Abdominal pain, dyspepsia, nausea, and tremor may occur.

Inhalation solution product (Perforomist) is indicated for COPD in adults (20 mcg Q12 hr; **max. dose** of 40 mcg/24 hr [20 mcg spaced 12 hr apart]).

**WARNING: Long-acting  $\beta_2$ -agonists may increase risk of asthma-related death.** Only use formoterol as additional therapy for patients not adequately controlled on other asthma-controller medications (e.g., low- to medium-dose inhaled corticosteroids) or whose disease severity clearly requires initiation of treatment with 2 maintenance therapies. Should **not** be used in conjunction with an inhaled long-acting  $\beta_2$ -agonist, and is **not** a substitute for inhaled or systemic corticosteroids. See Chapter 24 for recommendations for asthma controller therapy.

**FOSCARNET**

Foscavir and generics

**Antiviral agent**



**Injection:** 24 mg/mL (250, 500 mL)

**HIV positive or exposed with the following infection (IV):**



**CMV disease:**

**Infant and child:**

**Induction:** 180 mg/kg/24 hr  $\div$  Q8 hr in combination with ganciclovir; continue until symptom improvement and convert to maintenance therapy

**Maintenance:** 90–120 mg/kg/dose Q24 hr

**CMV retinitis (disseminated disease):**

**Infant and child:**

**Induction:** 180 mg/kg/24 hr  $\div$  Q8 hr  $\times$  14–21 days with or without ganciclovir

**Maintenance:** 90–120 mg/kg/24 hr once daily

**Adolescent and adult:**

**Induction:** 180 mg/kg/24 hr  $\div$  Q8–12 hr  $\times$  14–21 days

**Maintenance:** 90–120 mg/kg/24 hr once daily

**Acyclovir-resistant herpes simplex:**

**Infant and child:** 40 mg/kg/dose Q8 hr or 60 mg/kg/dose Q12 hr for up to 3 wk or until lesions heal

**Adolescent and adult:** 40 mg/kg/dose Q8–12 hr  $\times$  14–21 days or until lesions heal

**Varicella zoster unresponsive to acyclovir:**

**Infant and child:** 40–60 mg/kg/dose Q8 hr  $\times$  7–10 days

**Adolescent:** 90 mg/kg/dose Q12 hr

**Varicella zoster, progressive outer retinal necrosis:**

**Infant and child:** 90 mg/kg/dose Q12 hr in combination with ganciclovir IV and intravitreal foscarnet with or without ganciclovir

**Adolescent:** 90 mg/kg/dose Q12 hr in combination with IV ganciclovir and intravitreal foscarnet and/or ganciclovir

**Intravitreal route for progressive outer retinal necrosis (HIV positive or exposed):**

**Child and adolescent:** 1.2 mg/0.05 mL per dose twice weekly in combination with IV foscarnet and ganciclovir and/or intravitreal ganciclovir

FOSCARNET *continued*

**Use with caution** in patients with renal insufficiency. **Discontinue use** in adults if serum Cr  $\geq$  2.9 mg/dL. **Adjust dose in renal failure** (see Chapter 31).



May cause peripheral neuropathy, seizures, hallucinations, GI disturbance, increased LFTs, hypertension, chest pain, ECG abnormalities, coughing, dyspnea, bronchospasm, and renal failure (adequate hydration and avoiding nephrotoxic medications may reduce risk). Hypocalcemia (increased risk if given with pentamidine), hypokalemia, and hypomagnesemia may also occur. Use with ciprofloxacin may increase risk for seizures.

**FOSPHENYTOIN**

Cerebyx and generics

**Anticonvulsant**



Yes



Yes



3



D

**Injection:** 50 mg phenytoin equivalent (75 mg fosphenytoin)/1 mL (2, 10 mL)  
1 mg phenytoin equivalent provides 0.0037 mmol phosphate.

**All doses are expressed as phenytoin sodium equivalents (PE) (see remarks for dose administration information):**



**Child:** See Phenytoin and use the conversion of 1 mg phenytoin = 1 mg PE.

**Adult:**

**Loading dose:**

**Status epilepticus:** 15–20 mg PE/kg IV

**Nonemergent loading:** 10–20 mg PE/kg IV/IM

**Nonemergent initial maintenance dose:** 4–6 mg PE/kg/24 hr IV/IM  $\div$  once daily or BID

**All doses should be prescribed and dispensed in terms of mg phenytoin sodium equivalents (PE) to avoid medication errors. Safety in pediatrics has not been fully established.**



**Use with caution** in patients with renal or hepatic impairment and porphyria (consider amount of phosphate delivered by fosphenytoin in patients with phosphate restrictions). Drug is also metabolized to liberate small amounts of formaldehyde, which is considered clinically insignificant with short-term use (e.g., 1 wk). Side effects: hypokalemia (with rapid IV administration), slurred speech, dizziness, ataxia, rash, exfoliative dermatitis, nystagmus, diplopia, and tinnitus. Increased unbound phenytoin concentrations may occur in patients with renal disease or hypoalbuminemia; measure “free” or “unbound” phenytoin levels in these patients.

Abrupt withdrawal may cause status epilepticus. BP and ECG monitoring should be present during IV loading-dose administration. **Max. IV infusion rate:** 3 mg PE/kg/min up to a **max.** of 150 mg PE/min.

Administer IM via 1 or 2 injection sites; IM route is **not recommended** in status epilepticus.

Therapeutic levels: 10–20 mg/L (free and bound phenytoin) *OR* 1–2 mg/L (free only). Recommended peak serum sampling times: 4 hr after an IM dose or 2 hr after an IV dose.

See *Phenytoin* remarks for drug interactions and additional side effects. Drug is more safely administered via peripheral IV than phenytoin.

**FUROSEMIDE**

Lasix and many generics

**Loop diuretic**

Yes



Yes



3



C/D

**Tab:** 20, 40, 80 mg**Injection:** 10 mg/mL (2, 4, 10 mL)**Oral solution:** 10 mg/mL (60, 120 mL), 40 mg/5 mL (5, 500 mL)**IM, IV:****Neonate (see remarks):** 0.5–1 mg/kg/dose Q8–24 hr; **max. dose** 2 mg/kg/dose**Infant and child:** 1–2 mg/kg/dose Q6–12 hr**Adult:** 20–40 mg/24 hr ÷ Q6–12 hr; **max. dose** 600 mg/24 hr or 80 mg/dose**PO:****Neonate:** Bioavailability by this route is poor; doses of 1–4 mg/kg/dose once daily to BID have been used.**Infant and child:** Start at 2 mg/kg/dose; may increase by 1–2 mg/kg/dose no sooner than 6–8 hr after the previous dose. **Max. dose:** 6 mg/kg/dose. Dosages have ranged from 1–6 mg/kg/dose Q12–24 hr.**Adult:** 20–80 mg/dose Q6–12 hr; **max. dose** 600 mg/24 hr.**Continuous IV infusion:****Infant and child:** Start at 0.05 mg/kg/hr and titrate to effect.**Adult:** Start at 0.1 mg/kg/hr and titrate to effect; **max. dose** 0.4 mg/kg/hr.

**Contraindicated** in anuria and hepatic coma. **Use with caution** in hepatic disease (hepatic encephalopathy has been reported); cirrhotic patients may require higher doses than usual. Ototoxicity may occur in presence of renal disease (especially when used with aminoglycosides), with rapid IV injection (do not infuse >4 mg/min in adults), or with hypoproteinemia. May cause hypokalemia, alkalosis, dehydration, hyperuricemia, and increased calcium excretion. Prolonged use in premature infants and in children <4 yr may result in nephrocalcinosis. May increase risk for PDA in premature infants during the first week of life.

Furosemide-resistant edema in pediatric patients may benefit with the addition of metolazone. Some of these patients may have an exaggerated response, leading to hypovolemia, tachycardia, and orthostatic hypotension requiring fluid replacement. Severe hypokalemia has been reported with a tendency for diuresis persisting for up to 24 hr after discontinuing metolazone.

**Max. rate of intermittent IV dose:** 0.5 mg/kg/min. For patients receiving ECMO, **do not** administer IV doses directly into the ECMO circuit; medication is absorbed in the circuit, which may result in diminished effects and the need for higher doses.

Pregnancy category changes to “D” if used in pregnancy-induced hypertension.

**GABAPENTIN**

Neurontin, Gralise, Horizant, and generics

**Anticonvulsant**

No



Yes



2



C

**Caps:** 100, 300, 400 mg**Tab:** 300, 600, 800 mg

**Slow-release/extended-release tabs** (these dosage forms are **not** interchangeable with other gabapentin products; different pharmacokinetic profiles affect dosing interval [see specific product information for specific indications for use and dosage]):

Gralise: 300, 600 mg

Horizant (Gabapentin Enacarbil): 300, 600 mg

**Oral solution:** 250 mg/5 mL (470 mL)

GABAPENTIN *continued***Seizures (maximum time between doses should not exceed 12 hr):****3–12 yr (PO [see remarks]):**

**Day 1:** 10–15 mg/kg/24 hr ÷ TID, then gradually titrate dose upward to the following dosages over a 3-day period:

**3–4 yr:** 40 mg/kg/24 hr ÷ TID

**≥5–12 yr:** 25–35 mg/kg/24 hr ÷ TID

**Dosages up to 50 mg/kg/24 hr have been well tolerated.**

**>12 yr and adults (PO [see remarks]):** Start with 300 mg TID; if needed, increase dose up to 1800 mg/24 hr ÷ TID. Usual effective doses: 900–1800 mg/24 hr ÷ TID. Doses as high as 3.6 g/24 hr have been tolerated.

**Neuropathic pain:****Child (PO [limited data]):**

**Day 1:** 5 mg/kg/dose at bedtime

**Day 2:** 5 mg/kg/dose BID

**Day 3:** 5 mg/kg/dose TID, then titrate dose to effect. Usual dosage range: 8–35 mg/kg/24 hr.

**Maximum daily dose has not been evaluated.**

**Adult (PO):**

**Day 1:** 300 mg at bedtime

**Day 2:** 300 mg BID

**Day 3:** 300 mg TID; then titrate dose to effect. Usual dosage range: 1800–2400 mg/24 hr; **max. dose** 3600 mg/24 hr.

**Postherpetic neuralgia:** The above dosage regimen may be titrated up PRN for pain relief to a daily dose of 1800 mg/24 hr ÷ TID (efficacy has been shown from 1800–3600 mg/24 hr, but no additional benefit has been shown for doses >1800 mg/24 hr). The Gralise dosage form is designed for once-daily administration with the evening meal, whereas the Horizant dosage form is dosed once daily–BID. See specific product information for details.

Generally used as adjunctive therapy for partial and secondary generalized seizures and neuropathic pain.



Somnolence, dizziness, ataxia, fatigue, and nystagmus were common in use for seizures (≥12 yr).

Viral infections, fever, nausea and/or vomiting, somnolence, and hostility have been reported in patients 3–12 yr receiving other antiepileptic drugs (AEDs). Dizziness, somnolence, and peripheral edema are common side effects in adults with postherpetic neuralgia. Suicidal behavior or ideation and multiorgan hypersensitivity (DRESS) have been reported.

**Do not withdraw medication abruptly** (withdraw gradually over a minimum of 1 wk). Drug is not metabolized by the liver and is primarily excreted unchanged in urine. Higher doses may be required for children <5 yr because of faster clearance in this age group.

May be taken with or without food. In TID dosing schedule, **interval between doses should not exceed 12 hr. Adjust dose in renal impairment (see Chapter 31).**



**GANCICLOVIR**

Cytovene, Vitrasert, Zirgan, and others

**Antiviral agent**

No



Yes



3



C

**Injection:** 500 mg; contains 4 mEq Na per 1 g drug**Intravitreal implant (sustained release over 5–8 mo):**

Vitrasert: 4.5 mg

**Ophthalmic gel (drops):**

Zirgan: 0.15% (5 g); contains benzalkonium chloride

**Cytomegalovirus (CMV) infections:****Neonate (congenital CMV):** 12 mg/kg/24 hr ÷ Q12 hr IV × 6 wk**Child > 3 mo and adult:****Induction therapy (duration 14–21 days):** 10 mg/kg/24 hr ÷ Q12 hr IV**IV maintenance therapy:** 5 mg/kg/dose once daily IV for 7 days/wk *OR* 6 mg/kg/dose once daily IV for 5 days/wk**Prevention of CMV in transplant recipients:****Child and adult:****Induction therapy (duration 7–14 days):** 10 mg/kg/24 hr ÷ Q12 hr IV**IV maintenance therapy:** 5 mg/kg/dose once daily IV for 7 days/wk *OR* 6 mg/kg/dose once daily IV for 5 days/wk for 100–120 days posttransplant**Prevention of CMV in HIV-infected individuals (see [www.aidsinfo.nih.gov](http://www.aidsinfo.nih.gov) for latest recommendations and guidelines for CMV treatment as well):****Recurrence prophylaxis:****Infant, child, adolescent and adult:** 5 mg/kg/dose IV once daily. Consider valganciclovir as an oral alternative.**CMV retinitis (intravitreal implant):****≥ 9 yr and adult:** One implant lasts for 5–8 mo. As drug is depleted from implant, retinitis will progress; implant may be removed and replaced.**Herpetic keratitis (ophthalmic gel/drops):****≥ 2 yr and adult:** Apply 1 drop onto affected eye(s) 5 times a day (≈ Q3 hr while awake) until corneal ulcer is healed, then 1 drop TID × 7 days.

Limited experience with use in children < age 12. **Contraindicated** in severe neutropenia (ANC < 500/microliter) or severe thrombocytopenia (platelets < 25,000/microliter). **Use with extreme caution. Reduce dose in renal failure (see Chapter 31).** For oral route of administration, see *Valganciclovir*.

Common side effects: Neutropenia, thrombocytopenia, retinal detachment, confusion. Drug reactions alleviated with dose reduction or temporary interruption. Ganciclovir may increase didanosine and zidovudine levels, whereas didanosine and zidovudine may decrease ganciclovir levels. Immunosuppressive agents may increase hematologic toxicities. Amphotericin B and cyclosporine and tacrolimus increases risk for nephrotoxicity. Imipenem/cilastatin may increase risk for seizures. Minimal dilution is 10 mg/mL and should be infused IV over ≥ 1 hr. IM and SC administration are **contraindicated** because of high pH (pH = 11).

**GCSF**

See Filgrastim

**GENTAMICIN**

Garamycin and many generics

**Antibiotic, aminoglycoside**

No



Yes



2



C/D

**Injection:** 10 mg/mL (2 mL), 40 mg/mL (2, 20 mL); some products may contain sodium metabisulfite**Premixed injection in NS:** 40 mg (50 mL), 60 mg (50 mL), 70 mg (50 mL), 80 mg (50, 100 mL), 90 mg (100 mL), 100 mg (50, 100 mL), 120 mg (50, 100 mL)**Ophthalmic ointment:** 0.3% (3.5 g)**Ophthalmic drops:** 0.3% (5, 15 mL)**Topical ointment:** 0.1% (15, 30 g)**Topical cream:** 0.1% (15, 30 g)**Initial empirical dosage; patient-specific dosage defined by therapeutic drug monitoring (see remarks):****Parenteral (IM or IV):****Neonate/Infant (see table below):**

Postconceptional Age (wk)	Postnatal Age (days)	Dose (mg/kg/dose)	Interval (hr)
≤29*	0–7	5	48
	8–28	4	36
	>28	4	24
30–33	0–7	4.5	36
	>7	4	24
34–37	0–7	4	24
	>7	4	18–24
≥38	0–7	4	24†
	>7	4	12–18

\*Or significant asphyxia, PDA, indomethacin use, poor cardiac output, reduced renal function.

†Use Q36 hr interval for HIE patients receiving whole-body therapeutic cooling.

**Child:** 7.5 mg/kg/24 hr ÷ Q8 hr**Adult:** 3–6 mg/kg/24 hr ÷ Q8 hr**Cystic Fibrosis:** 7.5–10.5 mg/kg/24 hr ÷ Q8 hr**Intrathecal/intraventricular (use preservative-free product only):****Newborn:** 1 mg once daily**>3 mo:** 1–2 mg once daily**Adult:** 4–8 mg once daily**Ophthalmic ointment:** Apply Q8–12 hr**Ophthalmic drops:** 1–2 drops Q2–4 hr

**Use with caution** in patients receiving anesthetics or neuromuscular blocking agents, and in patients with neuromuscular disorders. May cause nephrotoxicity and ototoxicity. Ototoxicity may be potentiated with the use of loop diuretics. Eliminated more quickly in patients with cystic fibrosis, neutropenia, and burns. **Adjust dose in renal failure (see Chapter 31).** Monitor peak and trough levels.

Therapeutic peak levels are 6–10 mg/L in general, and 8–10 mg/L in pulmonary infections, cystic fibrosis, neutropenia, osteomyelitis, and severe sepsis.

To maximize bactericidal effects, an individualized peak concentration to target a peak/MIC ratio of 8–10:1 may be applied.

Therapeutic trough levels: <2 mg/L. Recommended serum sampling time at steady state: trough within 30 min before third consecutive dose, and peak 30–60 min after administration of third consecutive dose.

For initial dosing in obese patients, use an adjusted body weight (ABW). ABW = Ideal body weight + 0.4 (Total body weight – Ideal body weight).

Pregnancy category is "C" for ophthalmic use and "D" with IV use.



**GLUCAGON HCl**

GlucaGen, Glucagon Emergency Kit

**Antihypoglycemic agent**

No



No



?



B

**Injection:** 1 mg vial (requires reconstitution)

1 unit = 1 mg

**Hypoglycemia (IM, IV, SC):****Neonate, infant, and child < 20 kg:** 0.5 mg/dose (or 0.02–0.03 mg/kg/dose) Q20 min PRN**Child ≥ 20 kg and adult:** 1 mg/dose Q20 min PRN**β-Blocker and calcium channel blocker overdose:** Load with 0.05–0.15 mg/kg (usually ≈ 10 mg in adults) IV over 1 min, followed by an IV infusion of 0.05–0.1 mg/kg/hr.

Alternatively, 5-mg IV bolus Q5–10 min PRN up to 4 doses. If patient is responsive at a particular bolus dose, initiate an hourly IV infusion at that same responsive dose (e.g., if patient responded at 10 mg, start infusion of 10 mg/hr).

**Use with caution** in insulinoma and/or pheochromocytoma. Drug product is genetically engineered and identical to human glucagon. High doses have cardiac stimulatory effect and have had some success in β-blocker and calcium channel blocker overdose. May cause nausea, vomiting, urticaria, and respiratory distress. **Do not delay** glucose infusion; dose for hypoglycemia is 2–4 mL/kg of dextrose 25%.

Onset of action: IM, 8–10 min; IV, 1 min. Duration of action: IM, 12–27 min; IV, 9–17 min.

**GLYCERIN**

Pedia-Lax, Sani-Supp, Fleet Liquid Supp, and others

**Osmotic Laxative**

No



No



?



C

**Rectal solution [OTC]:** 4 mL per application (6 doses), 7.5 mL per application (4 doses)**Suppository [OTC]:**

Infant/pediatric: 1, 1.2 g (10s, 12s, 25s)

Adult: 2 g (10s, 12s, 24s, 25s, 50s)

**Constipation:****Neonate:** 0.5 mL/kg/dose rectal solution PR as an enema once daily PRN or half of infant suppository PR once daily PRN**Child < 6 yr:** 2–5 mL rectal solution PR as an enema or 1 infant suppository PR once daily PRN**> 6 yr–adult:** 5–15 mL rectal solution PR as an enema or 1 adult suppository PR once daily PRN**Onset of action:** 15–30 min. May cause rectal irritation, abdominal pain, bloating, and dizziness. Insert suppository high into rectum and retain for 15 min.**GLYCOPYRROLATE**

Robinul, Cuvposa, Glycate, and generics

**Anticholinergic agent**

Yes



Yes



?



B/C

**Tabs:** 1, 1.5, 2 mg**Oral solution (Cuvposa):** 1 mg/5 mL; contains propylene glycol and parabens**Injection:** 0.2 mg/mL (1, 2, 5, 20 mL); some multidose vials contain 0.9% benzyl alcohol**Respiratory antisecretory:****IM/IV:****Child:** 0.004–0.01 mg/kg/dose Q4–8 hr

GLYCOPYRROLATE *continued***Adult:** 0.1–0.2 mg/dose Q4–8 hr**Max. dose:** 0.2 mg/dose or 0.8 mg/24 hr**Oral:****Child:** 0.04–0.1 mg/kg/dose Q4–8 hr**Adult:** 1–2 mg/dose BID–TID**Reverse neuromuscular blockade:****Child and adult:** 0.2 mg IV for every 1 mg neostigmine or 5 mg pyridostigmine

**Use with caution** in hepatic and renal disease, ulcerative colitis, asthma, glaucoma, ileus, or urinary retention. Atropine-like side effects: tachycardia, nausea, constipation, confusion, blurred vision, and dry mouth. These may be potentiated if given with other drugs with anticholinergic properties.



Onset of action: PO, within 1 hr; IM/SC, 15–30 min; IV, 1 min. Duration of antisialogogue effect: PO, 8–12 hr; IM/SC/IV, 7 hr.

Pregnancy category is "B" for the injection and tablet dosage forms and "C" for the oral solution.

**GRANISETRON**

Kytril, Granisol, Sancuso, and generics

**Antiemetic agent, 5-HT<sub>3</sub> antagonist**

Yes



No



?



B

**Injection:** 1 mg/mL (1, 4 mL); 4-mL vials contain benzyl alcohol**Tabs:** 1 mg**Oral liquid (Granisol):** 0.2 mg/mL (30 mL); contains sodium benzoate**Transdermal patch (Sancuso):** 3.1 mg/24 hr**Chemotherapy-induced nausea and vomiting:****IV:**

**Child ≥ 2 yr and adult:** 10–20 mcg/kg/dose 15–60 min before chemotherapy; same dose may be repeated 2–3 times at ≥10-min intervals after chemotherapy (within 24 hr after chemotherapy) as a treatment regimen. **Max. dose:** 3 mg/dose or 9 mg/24 hr. Alternatively, a single 40-mcg/kg/dose 15–60 min before chemotherapy has been used.

**PO:**

**Adult:** 2 mg/24 hr ÷ once daily–BID; initiate first dose 1 hr before chemotherapy.

**Postoperative nausea and vomiting prevention (dosed before anesthesia or immediately before anesthesia reversal) and treatment (IV; see remarks):**

**Adult:** 1 mg × 1

**Radiation-induced nausea and vomiting prevention:**

**Adult:** 2 mg once daily PO administered 1 hr before radiation

**Transdermal patch:**

**Prophylaxis for chemotherapy-induced nausea and vomiting (adult):** Apply 1 patch 24–48 hr prior before chemotherapy. Patch may be worn up to 7 days, depending on chemotherapy regimen duration.

**Use with caution** in liver disease and preexisting cardiac conduction disorders and arrhythmias. May cause hypertension, hypotension, arrhythmias, agitation, and insomnia.



Inducers or inhibitors of the CYP 450 3A3/4 drug metabolizing enzymes may increase or decrease, respectively, the drug's clearance. QT prolongation has been reported.

Safety and efficacy in pediatric patients for prevention of postoperative nausea and vomiting has not been established owing to lack of efficacy and QT prolongation in a prospective multicenter randomized double-blinded trial in 157 patients (2–16 years old).

Onset of action: IV, 4–10 min. Duration of action: IV, ≤24 hr.

**GRISEOFULVIN**

Grifulvin V, Griseofulvin Microsize, Grisactin, Gris-PEG, and generics

**Antifungal agent**

Yes



No



?



C

**Microsize:****Tabs (Grifulvin V):** 500 mg**Oral suspension (Griseofulvin Microsize):** 125 mg/5 mL (120 mL); contains 0.2% alcohol, parabens, and propylene glycol**Ultramicronized (250 mg ultramicronized is  $\approx$  500 mg microsize):****Tabs (Gris-PEG):** 125, 250 mg**Microsize:****Child > 2 yr:** 10–20 mg/kg/24 hr PO  $\div$  once daily–BID; give with milk, eggs, fatty foods.

Some have recommended a higher dose of 20–25 mg/kg/24 hr PO for tinea capitis to improve efficacy, owing to relative resistance of the organism.

**Adult:** 500–1000 mg/24 hr PO  $\div$  once daily–BID**Max. dose (all ages):** 1 g/24 hr**Ultramicronized:****Child > 2 yr:** 10–15 mg/kg/24 hr PO  $\div$  once daily–BID**Adult:** 330–750 mg/24 hr PO  $\div$  once daily–BID**Max. dose (all ages):** 750 mg/24 hr**Contraindicated** in porphyria, pregnancy, and hepatic disease. Monitor hematologic, renal, and hepatic function. May cause leukopenia, rash, headache, paresthesias, and GI symptoms.

Severe skin reactions (e.g., Stevens-Johnson syndrome, TEN), erythema multiforme, LFT elevations (AST, ALT, bilirubin), and jaundice have been reported. Possible cross-reactivity in penicillin-allergic patients. Usual treatment period is 8 wk for tinea capitis and 4–6 mo for tinea unguium. Photosensitivity reactions may occur. May reduce effectiveness or decrease level of oral contraceptives, warfarin, and cyclosporine. Induces CYP 450 1A2 isoenzyme. Phenobarbital may enhance clearance of griseofulvin. Coadministration with fatty meals will increase drug's absorption.

**GUANFACINE**

Intuniv, Tenex, and generics

 **$\alpha_2$ -Adrenergic agonist**

Yes



Yes



3



B

**Tabs:** 1, 2 mg**Extended-release tabs:** 1, 2, 3, 4 mg**Attention deficit hyperactivity disorder (see remarks):****Immediate-release tab:** **$\geq 6$  yr and adolescent:** **$\leq 45$  kg:** Start at 0.5 mg QHS; if needed and tolerated, increase dose every 3–4 days at 0.5 mg/24-hr increments by increasing dosing frequency to BID, TID, QID. **Max. dose:** 27–40.5 kg: 2 mg/24 hr and 40.5–45 kg: 3 mg/24 hr. **$> 45$  kg:** Start at 1 mg QHS; if needed and tolerated, increase dose every 3–4 days at 1 mg/24-hr increments by increasing dosing frequency to BID, TID, QID. **Max. dose:** 4 mg/24 hr.**Extended-release tab:****6–17 yr:** Start at 1 mg Q24 hr; if needed and tolerated, increase dose no more than 1 mg/wk up to **max. dose** of 4 mg/24 hr.

GUANFACINE *continued***Use with strong CYP 450 3A4 inhibitors or inducers:**

CYP 450 3A4 characteristic	Adding guanfacine with respective CYP 450 3A4 inducer/inhibitor already on board.	Adding respective CYP 450 3A4 inducer/inhibitor with guanfacine already on board.
Strong inducer (e.g., carbamazepine, phenytoin, rifampin, St. John's Wort)	Guanfacine may be titrated faster at 2 mg/wk; if needed and tolerated, up to a <b>max.</b> of 8 mg/24 hr.	Gradually double original guanfacine dose over 1–2 wk as tolerated. When the strong inducer is discontinued, decrease guanfacine dose by 50% over 1–2 weeks ( <b>max. dose</b> 4 mg/24 hr).
Strong inhibitor (e.g., clarithromycin, azole antifungals)	Use lower <b>max.</b> daily guanfacine dose of 2 mg/24 hr.	Decrease guanfacine dose by 50%. When the strong inhibitor is discontinued, double the guanfacine dose ( <b>max. dose</b> 4 mg/24 hr).

**Use with caution** in patients at risk for hypotension, bradycardia, heart block, and syncope. A dose-dependent hypotension and bradycardia may occur. Orthostatic hypotension and syncope have been reported. Somnolence, fatigue, insomnia, dizziness, and abdominal pain are common side effects.



Drug is a substrate for CYP 450 3A4. See dosing section for dosage adjustment with inhibitors and inducers.

**Do not** abruptly discontinue therapy. Dose reductions may be required with clinically significant renal or hepatic impairment. When converting from immediate-release tabs to extended-release tabs, **do not** convert on a mg-per-mg basis (there are differences in pharmacokinetic profiles), but discontinue the immediate-release, and titrate with the extended-release product using the recommended dosing schedule.

**HALOPERIDOL**

Haldol, Haldol Decanoate, and generics

**Antipsychotic agent**



Yes



Yes



3



C

**Injection (IM use only):**

Lactate: 5 mg/mL (1, 10 mL); may contain parabens

Decanoate (long-acting): 50, 100 mg/mL (1, 5 mL); in sesame oil with 1.2% benzyl alcohol

**Tabs:** 0.5, 1, 2, 5, 10, 20 mg

**Oral solution:** 2 mg/mL (15, 120 mL)

**Child 3–12 yr:**

**PO:** Initial dose at 0.025–0.05 mg/kg/24 hr ÷ BID–TID. If necessary, increase daily dosage by 0.25–0.5 mg/24 hr Q5–7 days PRN up to a **max. dose** of 0.15 mg/kg/24 hr. Usual maintenance doses for specific indications include:

**Agitation:** 0.01–0.03 mg/kg/24 hr once daily PO

**Psychosis:** 0.05–0.15 mg/kg/24 hr ÷ BID–TID PO

**Tourette syndrome:** 0.05–0.075 mg/kg/24 hr ÷ BID–TID PO; may increase daily dose by 0.5 mg Q5–7 days

**IM, as lactate, for 6–12 yr:** 1–3 mg/dose Q4–8 hr; **max. dose** 0.15 mg/kg/24 hr

**>12 yr:**

**Acute agitation:** 2–5 mg/dose IM as lactate *OR* 1–15 mg/dose PO; repeat in 1 hr PRN

**Psychosis:** 2–5 mg/dose Q4–8 hr IM PRN *OR* 1–15 mg/24 hr ÷ BID–TID PO

**Tourette syndrome:** 0.5–2 mg/dose BID–TID PO; 3–5 mg/dose BID–TID PO may be used for severe symptoms



*Continued*

HALOPERIDOL *continued*

**Use with caution** in patients with cardiac disease (risk of hypotension), renal or hepatic dysfunction, thyrotoxicosis, and in patients with epilepsy (drug lowers the seizure threshold). Extrapyramidal symptoms, drowsiness, headache, tachycardia, ECG changes, nausea, and vomiting can occur. Higher-than-recommended doses are associated with a higher risk of QT prolongation and torsades de pointes. Leukopenia/neutropenia, including agranulocytosis, has been reported.

Drug is metabolized by CYP 450 1A2, 2D6, and 3A3/4 isoenzymes. May also inhibit CYP 450 2D6 and 3A3/4 isoenzymes. Serotonin-specific reuptake inhibitors (e.g., fluoxetine) may increase levels and effects of haloperidol. Carbamazepine and phenobarbital may decrease levels and effects of haloperidol. Monitor for encephalopathic syndrome when used in combination with lithium.

Acutely aggravated patients may require doses as often as Q60 min. **Decanoate salt is given every 3–4 wk in doses that are 10–15 times the individual patient's stabilized oral dose.**

**HEPARIN SODIUM**

Various generics

**Anticoagulant**



No



No



1



C

**Injection:**

Porcine intestinal mucosa: 1000, 2500, 5000, 10,000, 20,000 U/mL (Some products may be preservative-free; multidose vials contain benzyl alcohol.)

**Lock flush solution (porcine based):** 1, 10, 100 U/mL (Some products may be preservative-free or contain benzyl alcohol.)

**Injection for IV infusion (porcine based):**

D<sub>5</sub>W: 40 U/mL (500 mL), 50 U/mL (500 mL), 100 U/mL (100, 250 mL); contains bisulfite

NS (0.9% NaCl): 2 U/mL (500, 1000 mL)

0.45% NaCl: 50 U/mL (250, 500 mL), 100 U/mL (250 mL); contains EDTA

120 U = approximately 1 mg

**Anticoagulation empirical dosage (see Chapter 14 for dosage adjustments):**

Continuous IV infusion (initial doses for goal *unfractionated* heparin (UFH) anti-Xa level of 0.3–0.7 units/mL):

Age	Loading Dose (IV)*	Initial IV Infusion Rate (units/kg/hr)
Neonate and infant < 1 yr	75 U/kg IV	28
Child ≤ 1–16 yr	75 U/kg IV ( <b>max. dose</b> 7700 U)	20 (max. initial rate: 1650 U/hr)
>16 yr	70 U/kg IV ( <b>max. dose</b> 7700 U)	15 (max. initial rate: 1650 U/hr)

\*Do not give loading dose for stroke patients, and obtain aPTT 4 hr after loading dose.

**DVT or PE prophylaxis:**

**Adult:** 5000 U/dose SC Q8–12 hr until ambulatory

**Heparin flush (doses should be less than heparinizing dose):**

**Younger child:** Lower doses should be used to avoid systemic heparinization.

**Older child and adult:**

**Peripheral IV:** 1–2 mL of 10 U/mL solution Q4 hr

**Central lines:** 2–3 mL of 100 U/mL solution Q24 hr

**TPN (central line) and arterial line:** Add heparin to make final concentration of 0.5–1 U/mL.

**Contraindicated** in active major bleeding, known or suspected HIT, and concurrent epidural therapy. **Use with caution** if platelets <50,000/mm<sup>3</sup>. **Avoid** IM injections and other medications affecting platelet function (e.g., NSAIDs, ASA). Toxicities include bleeding, allergy, alopecia, and thrombocytopenia.

HEPARIN SODIUM *continued*

Adjust dose with one of the following laboratory goals:

*Unfractionated* heparin (UFH) anti-Xa level: 0.3–0.7 units/mL

aPTT level (reagent specific to reflect anti-Xa level of 0.3–0.7 units/mL): 50–80 seconds.

These laboratory measurements are best measured 4–6 hr after initiation or changes in infusion rate.

**Do not** collect blood levels from the heparinized line or same extremity as site of heparin infusion. If *unfractionated* heparin anti-Xa or aPTT levels are not available, a ratio of aPTT 1.5–2.5 times control value has been used in the past. *Unfractionated* heparin anti-Xa level is NOT THE SAME as *low-molecular-weight* heparin (LMWH) anti-Xa (used for monitoring LMWH products such as enoxaparin).

Use preservative-free heparin in neonates. **Note:** heparin flush doses may alter APTT in small patients; consider using more dilute heparin in these cases.

Use actual body weight when dosing obese patients. Due to recent regulatory changes to the manufacturing process, heparin products may exhibit decreased potency.

**Antidote:** protamine sulfate (1 mg per 100 U heparin in previous 4 hr). For LMWH, see *Enoxaparin*.

## HYALURONIDASE

Amphadase, Hylanex, Vitrase

**Antidote, extravasation**

**Injection:**

Amphadase: 150 U/mL (1 mL); bovine source and contains thimerosal

Hylanex: 150 U/mL (1 mL); recombinant human source; contains 1 mg albumin per 150 U

Vitrax: 200 U/mL (1.2 mL); ovine source, preservative-free

Pharmacy can make a 15 U/mL dilution.

**Infant and child:** Give 1 mL (150 U) by injecting 5 separate injections of 0.2 mL (30 U) at borders of extravasation site SC or intradermally, using a 25- or 26-gauge needle. Alternatively, a diluted 15 U/mL concentration has been used with the same dosing instructions.



**Contraindicated** in dopamine and  $\alpha$ -agonist extravasation and hypersensitivity to the respective product sources (bovine or ovine). May cause urticaria. Patients receiving large amounts of salicylates, cortisone, ACTH, estrogens, or antihistamines may decrease the effects of hyaluronidase (larger doses may be necessary). Administer as early as possible (minutes to 1 hour) after IV extravasation.



## HYDRALAZINE HYDROCHLORIDE

Apresoline and generics

**Antihypertensive, vasodilator**



**Tabs:** 10, 25, 50, 100 mg

**Injection:** 20 mg/mL (1 mL)

**Oral liquid:** 1.25, 4 mg/mL

Some dosage forms may contain tartrazines or sulfites.

**Hypertensive crisis (may result in severe and prolonged hypotension, see Chapter 4 for alternatives).**



**Child:** 0.1–0.2 mg/kg/dose IM or IV Q4–6 hr PRN; **max. dose** 20 mg/dose. Usual IV/IM dosage range is 1.7–3.5 mg/kg/24 hr

**Adult:** 10–40 mg IM or IV Q4–6 hr PRN

*Continued*



HYDRALAZINE HYDROCHLORIDE *continued***Chronic hypertension:**

**Infant and child:** Start at 0.75–1 mg/kg/24 hr PO ÷ Q6–12 hr (**max. dose** 25 mg/dose). If necessary, increase dose over 3–4 wk up to a **max. dose** of 5 mg/kg/24 hr for infants and 7.5 mg/kg/24 hr for children, or 200 mg/24 hr.

**Adult:** 10–50 mg/dose PO QID; **max. dose** of 300 mg/24 hr

**Use with caution** in severe renal and cardiac disease. Slow acetylators, patients receiving high-dose chronic therapy, and those with renal insufficiency are at highest risk of lupus-like syndrome (generally reversible). May cause reflex tachycardia, palpitations, dizziness, headaches, and GI discomfort. MAO inhibitors and  $\beta$ -blockers may increase hypotensive effects. Indomethacin may decrease hypotensive effects.

Drug undergoes first-pass metabolism. Onset of action: PO, 20–30 min; IV, 5–20 min. Duration of action: PO, 2–4 hr; IV, 2–6 hr. **Adjust dose in renal failure (see Chapter 31).**

**HYDROCHLOROTHIAZIDE**

Microzide, many generics, and previously available as Hydrodiuril  
**Diuretic, thiazide**



No



Yes



2



B/D

**Tabs:** 12.5, 25, 50 mg

**Caps (Microzide and generics):** 12.5 mg

**Edema:**

**Neonate and infant < 6 mo:** 2–4 mg/kg/24 hr ÷ BID PO; **max. dose** 37.5 mg/24 hr

**≥ 6 mo and child:** 2 mg/kg/24 hr ÷ BID PO; **max. dose** 100 mg/24 hr

**Adult:** 25–100 mg/24 hr ÷ once daily–BID PO; **max. dose** 200 mg/24 hr

**Hypertension:**

**Infant and child:** Start at 0.5–1 mg/kg/24 hr once daily PO; dose may be increased to a **max. dose** of 3 mg/kg/24 hr up to 50 mg/24 hr.

**Adult:** 12.5–25 mg/dose once daily–BID PO; doses >50 mg/24 hr often result in hypokalemia.

See *Chlorothiazide*. May cause fluid and electrolyte imbalances and hyperuricemia. Drug may not be effective when creatinine clearance is <25–50 mL/min. Use with carbamazepine may result in symptomatic hyponatremia.

Hydrochlorothiazide is also available in combination with potassium-sparing diuretics (e.g., spironolactone), ACE inhibitors, angiotensin II receptor antagonists, hydralazine, methyldopa, reserpine, and  $\beta$ -blockers.

Pregnancy category is "D" if used in pregnancy-induced hypertension.

**HYDROCORTISONE**

Solu-Cortef, Cortef, Cortifoam, Colocort, Cortenema, NuCort, and many others, including generics

**Corticosteroid**



No



No




3



C/D

**Hydrocortisone base:**

Tabs (Cortef and generics): 5, 10, 20 mg

Oral suspension: 1, 2, 2.5 mg/mL 

Rectal cream: 1% (30 g), 2.5% (30 g)

Rectal suspension (Colocort, Cortenema): 100 mg/60 mL (7s)

Topical ointment: 0.5% [OTC], 1% [OTC], 2.5%

HYDROCORTISONE *continued*

Topical cream: 0.5% [OTC], 1% [OTC], 2.5%

Topical lotion: 1% [OTC], 2.5%

**Na Succinate (Solu-Cortef):**

Injection: 100, 250, 500, 1000 mg/vial; contains benzyl alcohol

**Acetate:**

Topical ointment [OTC]: 0.5%, 1%

Topical cream [OTC]: 0.5%, 1%

Topical lotion (NuCort): 2% (60 g); contains benzyl alcohol

Rectal cream: 1%

Suppository: 25, 30 mg

Rectal foam aerosol (Cortifoam): 10% (90 mg/dose) (15 g)

**Status asthmaticus:****Child:**

**Loading dose (optional):** 4–8 mg/kg/dose IV; **max. dose** of 250 mg

**Maintenance:** 8 mg/kg/24 hr ÷ Q6 hr IV

**Adult:** 100–500 mg/dose Q6 hr IV

**Physiologic replacement:** see Chapter 10 for dosing.

**Anti-inflammatory/immunosuppressive:**

**Child:**

**PO:** 2.5–10 mg/kg/24 hr ÷ Q6–8 hr

**IM/IV:** 1–5 mg/kg/24 hr ÷ Q12–24 hr

**Adolescent and adult:**

**PO/IM/IV:** 15–240 mg/dose Q12 hr

**Acute adrenal insufficiency:** See Chapter 10 for dosing.

**Topical use:**

**Child and adult:** Apply to affected areas BID–QID, depending on severity.

**Rectal use:**

**Adolescent and adult:** Insert 1 application once daily–BID × 2–3 weeks.

**Use with caution** in immunocompromised patients; they should avoid exposure to chickenpox or measles.

For doses based on body surface area and topical preparations (with comparisons), see Chapters 10 and 30. Pregnancy category changes to "D" if used in first trimester.

**HYDROMORPHONE HCL**

Dilaudid, Dilaudid-HP, Exalgo, and generics

**Narcotic, analgesic**



Yes



Yes



3



C/D

**Tabs:** 2, 4, 8 mg

**Extended-release tabs (Exalgo):** 8, 12, 16, 32 mg

**Injection:** 1, 2, 4, 10 mg/mL (may contain methyl- and propylparabens)

**Powder for injection (Dilaudid-HP):** 250 mg

**Suppository:** 3 mg

**Oral solution:** 1 mg/mL

**Analgesia, initial doses (titrate to effect):**

**Child (<50 kg):**

**IV:** 0.015 mg/kg/dose Q4–6 hr PRN

**PO:** 0.03–0.08 mg/kg/dose Q4–6 hr PRN; **max. dose** 5 mg/dose

*Continued*

HYDROMORPHONE HCL *continued***Analgesia, initial doses (titrate to effect):****Adolescent (>50 kg) and adult:****IM, IV, SC:** 1–2 mg/dose Q4–6 hr PRN**PO:****Adolescent:** 1–2 mg/dose Q4–6 hr PRN**Adult:** 2–4 mg/dose Q4–6 hr PRN

**Refer to Chapter 6 for equianalgesic doses and for patient-controlled analgesia dosing.** Less pruritus than morphine. Similar profile of side effects to other narcotics. **Use with caution** in infants and young children, and **do not use** in neonates (potential CNS effects). Dose reduction recommended in renal insufficiency or severe hepatic impairment. Pregnancy category changes to "D" if used for prolonged periods or in high doses at term.

Extended-release tab use requires Risk Evaluation and Mitigation Strategies (REMS)-based provision of safety information and postmarketing safety studies.

**HYDROXYCHLOROQUINE**

Plaquenil and generics

**Antimalarial, antirheumatic agent**

Yes




Yes



2



?

**Tabs:** 200 mg (155 mg base)**Oral suspension:** 25 mg/mL (19.375 mg/mL base) **All doses expressed in mg of hydroxychloroquine base.****Malaria prophylaxis (start 2 wk before exposure and continue for 4 wk after leaving endemic area):****Child:** 5 mg/kg/dose PO once weekly; **max. dose** 310 mg**Adult:** 310 mg PO once weekly**Malaria treatment (acute uncomplicated cases):**For treatment of malaria, consult with ID specialist or see the latest edition of the AAP *Red Book*.**Child:** 10 mg/kg/dose (**max. dose** 620 mg) PO  $\times$  1, followed by 5 mg/kg/dose (**max. dose** 310 mg) 6 hr later. Then 5 mg/kg/dose (**max. dose** 310 mg) Q24 hr  $\times$  2 doses, starting 24 hr after first dose.**Adult:** 620 mg PO  $\times$  1, followed by 310 mg 6 hr later. Then 310 mg Q24 hr  $\times$  2 doses, starting 24 hr after first dose.**Juvenile rheumatoid arthritis or systemic lupus erythematosus:****Child:** 2.325–3.875 mg/kg/24 hr (base) PO  $\div$  once daily–BID; **max. dose** of 310 mg/24 hr, **not to exceed** 5.425 mg/kg/24 hr.

**Contraindicated** in psoriasis, porphyria, retinal or visual field changes, and 4-aminoquinoline hypersensitivity. **Use with caution** in liver disease, G6PD deficiency, concomitant hepatic toxic drugs, renal impairment, metabolic acidosis, or hematologic disorders.



Long-term use in children is **not recommended**. May cause headaches, myopathy, GI disturbances, skin and mucosal pigmentation, agranulocytosis, visual disturbances, and increased digoxin serum levels. Use with aurothioglucose may increase risk for blood dyscrasias.

When used in combination with other immunosuppressive agents for SLE and JRA, lower doses of hydroxychloroquine can be used.

Pregnancy category has not been formally assigned by the FDA. The only situation where use is recommended during pregnancy is during suppression or treatment of malaria, when benefits outweigh risks.

**HYDROXYZINE**

Vistaril and various generics

*Antihistamine, anxiolytic, antiemetic*

Yes



No



3



C

**Tabs (HCl salt):** 10, 25, 50 mg**Caps (pamoate salt):** 25, 50, 100 mg**Oral syrup, solution (HCl salt):** 10 mg/5 mL (120, 473 mL); may contain alcohol**Injection for IM use (HCl salt):** 25, 50 mg/mL; may contain benzyl alcohol**NOTE:** Pamoate and HCL salts are equivalent in regard to mg of hydroxyzine.**Pruritus and anxiety:****Oral:****Child:** 2 mg/kg/24 hr ÷ Q6–8 hr PRN**Max. single dose:**

&lt;6 yr: 12.5 mg,

6–12 yr: 25 mg

&gt;12 yr: 100 mg

**Alternative dosing by age:**

&lt;6 yr: 50 mg/24 hr ÷ Q6–8 hr PRN

≥6 yr: 50–100 mg/24 hr ÷ Q6–8 hr PRN

**Adult:** 25 mg/dose TID–QID PRN; **max. dose** 600 mg/24 hr**IM:****Child and adolescent:** 0.5–1 mg/kg/dose Q4–6 hr PRN; **max. single dose** 100 mg**Adult:** 25–100 mg/dose Q4–6 hr PRN; **max. dose** 600 mg/24 hr

May potentiate barbiturates, meperidine, and other CNS depressants. May cause dry mouth, drowsiness, tremor, convulsions, blurred vision, and hypotension. May cause pain at injection site.

Increase dosage interval to Q24 hr or less in the presence of liver disease (e.g., primary biliary cirrhosis).

Onset of action within 15–30 min. Duration of action 4–6 hr. IV administration is **not recommended**.**IBUPROFEN**

PO: Motrin, Advil, Children's Advil, Children's Motrin, and generics

IV: NeoProfen, Caldolor

*Nonsteroidal anti-inflammatory agent*

Yes



Yes



1



C/D

**Oral suspension [OTC]:** 100 mg/5 mL (60, 120, 480 mL)**Oral drops [OTC]:** 40 mg/mL (15, 30 mL)**Chewable tabs [OTC]:** 50, 100 mg**Caplets [OTC]:** 100, 200 mg**Tabs:** 100 [OTC], 200 [OTC], 400, 600, 800 mg**Capsules [OTC]:** 200 mg**Injection:****NeoProfen (lysine salt):** 10 mg ibuprofen base/1 mL (2 mL)**Caldolor:** 100 mg/mL (4, 8 mL); contains 78 mg/mL arginine**PO:****Infant and child (≥6 mo):****Analgesic/antipyretic:** 5–10 mg/kg/dose Q6–8 hr PO; **max. dose** 40 mg/kg/24 hr**JRA (6 mo–12 yr):** 30–50 mg/kg/24 hr ÷ Q6 hr PO; **max. dose** 2400 mg/24 hr

Continued

IBUPROFEN *continued***Adult:**

**Inflammatory disease:** 400–800 mg/dose Q6–8 hr PO; **max. dose** 800 mg/dose *OR* 3.2 g/24 hr

**Pain/fever/dysmenorrhea:** 200–400 mg/dose Q4–6 hr PRN PO; **max. dose** 1.2 g/24 hr

**IV:**

**Analgesic ( $\geq 17$  yr and adult [see remarks]):** 400–800 mg/dose Q6 hr PRN; **max. dose** 3200 mg/24 hr

**Antipyretic ( $\geq 17$  yr and adult [see remarks]):** 400 mg/dose Q4–6 hr or 100–200 mg/dose Q4 hr PRN; **max. dose** 3200 mg/24 hr

**Closure of ductus arteriosus:**

**<32 wk of gestation and 0.5–1.5 kg (use birth weight to calculate all doses and infuse all doses over 15 min [see remarks]):** 10 mg/kg/dose IV  $\times$  1, followed by 2 doses of 5 mg/kg/dose each after 24 and 48 hr. Hold second or third dose if urinary output is  $<0.6$  mL/kg/hr; dosing should resume when laboratory studies indicate return of normal renal function. If ductus arteriosus fails to close or reopens, a second course of ibuprofen, use of IV indomethacin, or surgery may be necessary.

**Contraindicated** with active GI bleeding and ulcer disease. **Use caution** with aspirin hypersensitivity, hepatic/renal insufficiency, heart disease (risk for MI and stroke with prolonged use), dehydration, and in patients receiving anticoagulants. GI distress (lessened with milk), rashes, ocular problems, hypertension, granulocytopenia, and anemia may occur. Inhibits platelet aggregation. Consumption of more than three alcoholic beverages per day or use with corticosteroids or anticoagulants may increase risk for GI bleeding.

May increase serum levels and effects of digoxin, methotrexate, and lithium. May decrease effects of antihypertensives, aspirin (antiplatelet effects), furosemide, and thiazide diuretics. Pregnancy category changes to "D" if used in third trimester or near delivery.

**IV USE for analgesia/antipyretic:** Hydrate patient well before use. Doses must be diluted to a concentration  $\leq 4$  mg/mL with NS, D<sub>5</sub>W, or LR and infused over  $\geq 30$  min. Most common reported side effects in clinical trials include nausea, flatulence, vomiting, and headache.

**IV USE for PDA:** **Contraindicated** in untreated infections, congenital heart diseases requiring a patent ductus arteriosus to facilitate satisfactory pulmonary and systemic blood flow, active intracranial or GI bleeds, thrombocytopenia, coagulation defects, suspected/active NEC, and significant renal impairment. **Use with caution** in hyperbilirubinemia. Not indicated for IVH prophylaxis. Renal side effects are generally less frequent and severe than with IV indomethacin.

**IMIPENEM AND CILASTATIN**

Primaxin IV and generics

**Antibiotic, carbapenem**



No



Yes



2



C

**Injection:** 250, 500 mg; contains 3.2 mEq Na/g drug

Each 1 mg drug contains 1 mg imipenem and 1 mg cilastatin.

**Neonate:**

**0–4 wk old and  $<1.2$  kg:** 50 mg/kg/24 hr  $\div$  Q12 hr IV

**$<1$  wk old and  $\geq 1.2$  kg:** 50 mg/kg/24 hr  $\div$  Q12 hr IV

**$\geq 1$  wk old and  $\geq 1.2$  kg:** 75 mg/kg/24 hr  $\div$  Q8 hr IV

**Child (4 wk–3 mo):** 100 mg/kg/24 hr  $\div$  Q6 hr IV

**Child ( $>3$  mo):** 60–100 mg/kg/24 hr  $\div$  Q6 hr IV; **max. dose** 4 g/24 hr

**Cystic fibrosis:** 90 mg/kg/24 hr  $\div$  Q6 hr IV; **max. dose** 4 g/24 hr

**Adult:**

**IV:** 1–4 g/24 hr  $\div$  Q6–8 hr; **max. dose** 4 g/24 hr or 50 mg/kg/24 hr, whichever is less

**IM:** 500–750 mg/dose Q12 hr

IMIPENEM AND CILASTATIN *continued*

For IV use, give slowly over 30–60 min at a concentration  $\leq 5$  mg/mL to reduce risk for nausea (lowering rate may reduce severity). Adverse effects: thrombophlebitis, pruritus, urticaria, GI symptoms, seizures, dizziness, hypotension, elevated LFTs, blood dyscrasias, and penicillin allergy. Greater risk for seizures may occur with CNS infections, concomitant use with ganciclovir, higher doses, and renal impairment. CSF penetration is variable but best with inflamed meninges.

**Do not administer with** probenecid (increases imipenem/cilastatin levels) and ganciclovir (increased risk for seizures). May significantly reduce valproic acid levels. **Adjust dose in renal insufficiency** (see Chapter 31).

**IMIPRAMINE**

Tofranil, Tofranil-PM, and many generics

**Antidepressant, tricyclic**



Yes



Yes



3



?

**Tabs (HCl):** 10, 25, 50 mg

**Caps (Tofranil-PM, pamoate):** 75, 100, 125, 150 mg; strengths are expressed as imipramine HCl equivalent.

**Antidepressant:****Child:**

**Initial:** 1.5 mg/kg/24 hr  $\div$  TID PO; increase 1–1.5 mg/kg/24 hr Q3–4 days to a **max. dose** of 5 mg/kg/24 hr.

**Adolescent:**

**Initial:** 25–50 mg/24 hr  $\div$  once daily–TID PO; **max. dose** 200 mg/24 hr. Dosages exceeding 100 mg/24 hr are generally not necessary.

**Adult:**

**Initial:** 75–100 mg/24 hr  $\div$  TID PO

**Maintenance:** 50–300 mg/24 hr QHS PO; **max. dose** 300 mg/24 hr

**Enuresis ( $\geq 6$  yr):**

**Initial:** 10–25 mg QHS PO

**Increment:** 10–25 mg/dose at 1- to 2-wk intervals until max. dose for age or desired effect achieved. Continue  $\times$  2–3 mo, then taper slowly.

**Max. doses:**

**6–12 yr:** 50 mg/24 hr

**$\geq 12$  yr:** 75 mg/24 hr

**Augment analgesia for chronic pain:**

**Initial:** 0.2–0.4 mg/kg/dose QHS PO; increase 50% Q2–3 days to a **max. dose** of 1–3 mg/kg/dose QHS PO.

**Contraindicated** in narrow-angle glaucoma and patients who used MAO inhibitors within 14 days. See Chapter 2 for management of toxic ingestion. Monitor for clinical worsening of depression and suicidal ideation/behavior after initiation of therapy or after dose changes.

**Use with caution** in renal or hepatic impairment. Side effects include sedation, urinary retention, constipation, dry mouth, dizziness, drowsiness, and arrhythmia. QHS dosing during first weeks of therapy will reduce sedation. Monitor ECG, BP, and CBC at start of therapy and with dose changes. Tricyclics may cause mania.

Therapeutic reference range (sum of imipramine and desipramine) = 150–250 ng/mL. Levels  $>1000$  ng/mL are toxic, but toxicity may occur at levels  $>300$  ng/mL.

Recommended serum sampling times at steady state: Obtain trough level within 30 min before next scheduled dose after 5–7 days of continuous therapy. Carbamazepine may reduce imipramine levels; cimetidine, fluoxetine, fluvoxamine, labetalol, and quinidine may increase imipramine levels.

*Continued*

IMIPRAMINE *continued*

Onset of antidepressant effects: 1–3 wk. **Do not discontinue abruptly** in patients receiving long-term high-dose therapy.

Pregnancy category has not been officially assigned by the FDA, but congenital anomalies have been reported in humans, with the causal relationship not established.

**IMMUNE GLOBULIN***Immune globulins*

No



Yes



?



C

**IM preparations:**

GamaSTAN S/D: 150–180 mg/mL (2, 10 mL); contains 0.21–0.32 M glycine; preservative free

**IV preparations in solution:**

Flebogamma DIF: 5% (50 mg/mL) (10, 50, 100, 200, 400 mL) 10% (100 mg/mL) (50, 100, 200 mL); contains 50 mg/mL sorbitol and  $\leq 6$  mg/mL polyethylene glycol; sucrose free

Gamunex-C: 10% (100 mg/mL) (10, 25, 50, 100, 200 mL); contains 0.16–0.24 M glycine; sucrose free

Gammagard liquid: 10% (100 mg/mL) (10, 25, 50, 100, 200 mL); contains 0.25 M glycine; sucrose free

Gammagard S/D  $\leq 1$  mcg/mL IgA: 5% (50 mg/mL) (100, 200 mL); contains 22.5 mg/mL glycine; sucrose and preservative free

Gammaked: 10% (100 mg/mL) (10, 25, 50, 100, 200 mL); contains 0.16–0.24 M glycine; sucrose free

Gamaplex: 5% (50 mg/mL) (50, 100, 200 mL); contains 50 mg/mL sorbitol, 6 mg/mL glycine, and 0.05 mg/mL polysorbate 80; sucrose free

Octagam: 5% (50 mg/mL) (20, 50, 100, 200, 500 mL); contains 100 mg/mL maltose; sucrose free

Privagen 10% (100 mg/mL) (50, 100, 200 mL); contains 210–290 mmol/L L-proline; sucrose free

**IV preparations in powder for reconstitution:**

Carimune NF: 3, 6, 12 g (contains 1.67 g sucrose and  $< 20$  mg NaCl per 1 g Ig); dilute to 3%, 6%, 9%, or 12%

Gammagard S/D: 2.5, 5, 10 g (contains 3 mg/mL albumin, 22.5 mg/mL glycine, 20 mg/mL glucose, 2 mg/mL polyethylene glycol, 1 mcg/mL tri-*n*-butyl phosphate, 1 mcg/mL octoxynol 9, and 100 mcg/mL polysorbate 80); dilute to 5% or 10%

**Subcutaneous (SC) preparations:**

Hizentra: 20% (200 mg/mL) (5, 10, 20 mL); contains 210–290 mmol/L L-proline, 10–30 mg/mL polysorbate 80; sucrose and preservative free

See indications and doses in Chapter 15.

**General guidelines for administration (see package insert of specific products):**

**IV:** Begin infusion at 0.01 mL/kg/min, double rate every 15–30 min, up to **max.** of 0.08 mL/kg/min.

If adverse reactions occur, stop infusion until side effects subside, and may restart at rate that was previously tolerated.

**Subcutaneous (SC) preparation:**

**Converting to SC route from previous IV dosage for patients receiving IV immune globulin (IVIG) infusions at regular intervals for at least 3 mo ( $\geq 2$  yr):**

**Initial weekly dose (start 1 wk after last IV dose):**

Dose (g) =  $1.53 \times \text{Previous IVIG dose in grams (g)} \div \text{number of weeks between IVIG doses}$

To convert the above dose in grams to milliliters of drug, multiply dose (g) by 5.

Adjust dose over time by clinical response and serum IgG trough levels. Obtain a previous trough level from IVIG therapy prior SC conversion, and repeat trough level 2–3 mo after initiating the SC route. A goal trough with the SC route of  $\approx 290$  mg/dL higher than a trough with the IV route has been recommended.

IMMUNE GLOBULIN *continued*

**SC administration:** Injection sites include abdomen, thigh, upper arm, and/or lateral hip. Doses may be administered into multiple sites (spaced  $\geq 2$  inches apart) simultaneously. See following table.

Subcutaneous Product	Max. Simultaneous Injection sites	Max. Infusion Rate	Max. Infusion Volume
Hizentra	4	First infusion: 15 mL/hr per infusion site Subsequent infusions: 25 mL/hr per infusion site (max. 50 mL/hr for all simultaneous sites combined)	First 4 infusions: 15 mL per infusion site Subsequent infusions: 20–25 mL per infusion site

**Use with caution** in patients with increased risk of thrombosis (e.g., hypercoagulable states, prolonged immobilization, indwelling catheters, estrogen use, thrombosis history, cardiovascular risks, and hyperviscosity) or hemolysis (e.g., non-O blood type, associated inflammatory conditions, and receiving high cumulative doses of immune globulins over several days).



May cause flushing, chills, fever, headache, and hypotension. Hypersensitivity reaction may occur when IV form is administered rapidly. Maltose containing products may cause an osmotic diuresis. May cause **anaphylaxis** in IgA-deficient patients due to varied amounts of IgA. Some products are IgA depleted; consult a pharmacist.

To decrease risk of renal dysfunction, including acute renal failure, IV preparations containing sucrose should not be infused at a rate such that the amount of sucrose exceeds 3 mg/kg/min.

SC route provides higher serum trough levels, lower rate of adverse reactions, and shorter administration time than IV route. Use of adjusted body weight [ABW=Ideal body weight + 0.5 (Actual body weight – Ideal body weight)] for dosing in obese patients has been recommended.

Delay immunizations after immune globulin administration (see latest AAP *Red Book* for details).

**INDOMETHACIN**

Indocin, Indocin SR, Indocin I.V., and various generics

**Nonsteroidal anti-inflammatory agent**



Yes



Yes



1



C/D

**Caps:** 25, 50 mg

**Sustained-release caps (Indocin SR and other generics):** 75 mg

**Oral suspension:** 25 mg/5 mL (237 mL); contains 1% alcohol

**Suppositories:** 50 mg (30s)

**Injection (Indocin I.V. and other generics):** 1 mg

**Anti-inflammatory/rheumatoid arthritis:**

**Child ( $\geq 2$  yr):** Start at 1–2 mg/kg/24 hr  $\div$  BID–QID PO; **max. dose** is the lesser of 4 mg/kg/24 hr or 200 mg/24 hr.

**Adult:** 50–150 mg/24 hr  $\div$  BID–QID PO; **max. dose** 200 mg/24 hr.

**Closure of ductus arteriosus:**

Infuse IV over 20–30 min:

Postnatal Age	Dose (mg/kg/dose Q12–24 hr)*		
	#1	#2	#3
<48 hr	0.2	0.1	0.1
2–7 days	0.2	0.2	0.2
>7 days	0.2	0.25	0.25

\*Do not administer if urine output is  $<0.6$  mL/kg/hr or anuric.

For infants  $<1500$  g, 0.1–0.2 mg/kg/dose IV Q24 hr may be given for an additional 3–5 days.

*Continued*



INDOMETHACIN *continued***Closure of ductus arteriosus:**

**Intraventricular hemorrhage prophylaxis:** 0.1 mg/kg/dose IV Q24 hr  $\times$  3 doses, initiated at 6–12 hr of age (give in consultation with a neonatologist).

**Contraindicated** in active bleeding, coagulation defects, necrotizing enterocolitis, and renal insufficiency (urine output  $< 0.6$  mL/kg/hr). **Use with caution** in cardiac dysfunction, hypertension, heart disease (risk for MI and stroke with prolonged use), and renal or hepatic impairment. May cause (especially in neonates) decreased urine output, platelet dysfunction (thrombocytopenia), decreased GI blood flow, and reduce antihypertensive effects of  $\beta$ -blockers, hydralazine, and ACE inhibitors. **Fatal hepatitis reported in treatment of JRA.** Monitor renal and hepatic function before and during use.

**Reduction in cerebral blood flow associated with rapid IV infusion;** infuse all IV doses over 20–30 min. Sustained-release capsules are dosed once daily–BID. Pregnancy category changes to "D" if used for  $>48$  hr or after 34-wk gestation or close to delivery.

**INSULIN PREPARATIONS****Pancreatic hormone**

Yes



Yes



1



B

Many preparations, at concentrations of 100, 500 U/mL. See Chapter 10.

Diluted concentrations of 1 U/mL or 10 U/mL may be necessary for smaller doses in neonates and infants.

**Hyperkalemia:** See Chapter 11.

**DKA:** See Chapter 10.

When using insulin drip with new IV tubing, fill tubing with insulin infusion solution and wait 30 min before connecting tubing to patient. Then flush the line and connect IV line to patient to start infusion. This will ensure proper drug delivery. **Adjust dose in renal failure (see Chapter 31).** **Use with caution** and monitor closely in hepatic impairment.

**IODIDE**

See Potassium Iodide

**IOHEXOL**

Omnipaque 140, Omnipaque 180, Omnipaque 240, Omnipaque 300, and Omnipaque 350

**Radiopaque agent, contrast media**



Yes



Yes



3



B

**Injection:**

Omnipaque 140: 302 mg iohexol equivalent to 140 mg iodine/mL (50 mL)

Omnipaque 180: 388 mg iohexol equivalent to 180 mg iodine/mL (10, 20 mL)

Omnipaque 240: 518 mg iohexol equivalent to 240 mg iodine/mL (10, 20, 50, 100, 150, 200 mL)

Omnipaque 300: 647 mg iohexol equivalent to 300 mg iodine/mL (10, 30, 50, 75, 100, 125, 150 mL)

Omnipaque 350: 755 mg iohexol equivalent to 350 mg iodine/mL (50, 75, 100, 125, 150, 200, 250 mL)

**Contrast-enhanced CT scan of abdomen:****Oral (administered before IV dose):**

**Child:** Mix 20 mL of Omnipaque 350 with 500 mL of noncarbonated beverage of patient's choice (apple juice works well for younger patients). Administer diluted contrast media PO 30–60 min before IV dose and image acquisition, using the following dosage:

**$<6$  mo:** 40–60 mL

**6–18 mo:** 120–160 mL

IOHEXOL *continued***18 mo–3 yr:** 165–240 mL**3 yr–12 yr:** 250–360 mL**>12 yr:** 480–520 mL

**Adult:** Mix 50 mL of Omnipaque 350 with half gallon of noncarbonated beverage of patient's choice. Give 2–4 cups containing 480 mL (16 oz) of diluted contrast media PO 20–40 min before IV dose and image acquisition.

**IV (administered after PO dose):**

**Child:** 1–2 mL/kg IV of Omnipaque 240 or Omnipaque 300 given 30–60 min after oral dose

**Max. dose:** 3 mL/kg

**Adult:** 100–150 mL IV of Omnipaque 300 given 20–40 min after oral dose

**Use with caution** in dehydration, previous allergic reaction to a contrast medium, iodine sensitivity, asthma, hay fever, food allergy, CHF, severe liver or renal impairment, diabetic nephropathy, multiple myeloma, pheochromocytoma, hyperthyroidism, and sickle cell disease. Allergic reactions, arrhythmias, and nephrotoxicity have been rarely reported. Children at higher risk for adverse events with contrast medium administration may include those with asthma, sensitivity to medication and/or allergens, CHF, serum creatinine > 1.5 mg/dL, or <12 mo.

Use **NOT** recommended with drugs that lower seizure threshold (e.g., phenothiazines), amiodarone (increased risk of cardiotoxicity), and metformin (lactic acidosis and acute renal failure).

Many other uses exist; see package insert for additional information. Iohexol is particularly useful when barium sulfate is **contraindicated** in patients with suspected bowel perforation or those where aspiration of contrast medium is of concern. Oral dose is poorly absorbed from the normal GI tract (0.1%–0.5%); absorption increases with bowel perforation or bowel obstruction. Concentrations 302–755 mg iohexol/mL have osmolalities from 1.1–3 times that of plasma (285 mOsm/kg) and CSF (301 mOsm/kg) and may be hypertonic.

**IPRATROPIUM BROMIDE**

Atrovent and generics

**Anticholinergic agent**



No



No



1



B

**Aerosol (HFA):** 17 mcg/dose (200 actuations per canister, 12.9 g)

**Nebulized solution:** 0.02% (500 mcg/2.5 mL) (25s, 30s, 60s)

**Nasal spray:** 0.03% (21 mcg per actuation, 30 mL); 0.06% (42 mcg per actuation, 15 mL)

**In combination with albuterol:**

Nebulized solution (DuoNeb): 0.5 mg ipratropium bromide and 2.5 mg albuterol in 3 mL (30s, 60s)

Aerosol (Combivent): 18 mcg ipratropium and 103 mcg albuterol per actuation (200 actuations per canister, 14.7 g)

Inhalation spray (Combivent Respimat): 20 mcg ipratropium and 100 mcg albuterol per actuation (120 actuations per canister, 4 g)

**Acute use in the ED or ICU:****Nebulizer treatments:**

**<12 yr:** 250 mcg/dose Q20 min × 3, then Q2–4 hr PRN

**≥12 yr:** 500 mcg/dose Q30 min × 3, then Q2–4 hr PRN

**Inhaler:**

**Child and adult:** 4–8 puffs PRN

**Nonacute use:****Inhaler:**

**<12 yr:** 1–2 puffs Q6 hr; **max. dose** 12 puffs/24 hr

**≥12 yr:** 2–3 puffs Q6 hr; **max. dose** 12 puffs/24 hr



*Continued*

IPRATROPIUM BROMIDE *continued***Non-acute use:****Nebulized treatments:***Infant:* 125–250 mcg/dose Q8 hr*Child ≤ 12 yr:* 250 mcg/dose Q6–8 hr*>12 yr and adult:* 250–500 mcg/dose Q6–8 hr**Nasal spray:****Allergic and nonallergic rhinitis:***≥6 yr and adult:* 2 sprays of 0.03% strength (42 mcg) per nostril BID–TID**Rhinitis associated with common cold (use up to a total of 4 days; safety and efficacy have not been evaluated >4 days):***5–11 yr:* 2 sprays of 0.06% strength (84 mcg) per nostril TID*≥12 yr and adult:* 2 sprays of 0.06% strength (84 mcg) per nostril TID–QID**Rhinitis associated with seasonal allergies (use up to a total of 3 weeks; safety and efficacy have not been evaluated >3 weeks):***≥5 yr and adult:* 2 sprays of 0.06% strength (84 mcg) per nostril QID**Contraindicated** in soy or peanut allergy (for aerosol inhaler) and atropine hypersensitivity.

**Use with caution** in narrow-angle glaucoma or bladder neck obstruction, though ipratropium has fewer anticholinergic systemic effects than atropine. May cause anxiety, dizziness, headache, GI discomfort, and cough with inhaler or nebulized use. Epistaxis, nasal congestion, and dry mouth/throat have been reported with nasal spray. Reversible anisocoria may occur with unintentional aerosolization of drug to eyes, particularly with mask nebulizers. Proven efficacy of nebulized solution in pediatrics is currently limited to reactive airway disease management in the ER and ICU areas. The combination product (Combivent) is currently approved for use only in adults and has not been studied in children.

Bronchodilation onset of action is 1–3 min, with peak effects within 1.5–2 hr and duration of action of 4–6 hr. Shake inhaler well before use with spacer. Nebulized solution may be mixed with albuterol (or use DuoNeb). Breast-feeding safety **extrapolated** from safety of atropine.

**IRON DEXTRAN**

See Iron – Injectable Preparations

**IRON SUCROSE**

See Iron – Injectable Preparations

**IRON—INJECTABLE PREPARATIONS**

Ferric gluconate: Ferlecit and generics

Iron dextran: INFeD, DexFerrum

Iron sucrose: Venofer

**Parenteral iron****Injection:**

Ferric gluconate (Ferlecit and generics): 62.5 mg/mL (12.5 mg elemental Fe/mL) (5 mL); contains 9 mg/mL benzyl alcohol and 20% sucrose.

Iron dextran (INFeD, DexFerrum): 50 mg/mL (50 mg elemental Fe/mL) (1, 2 mL); products containing phenol 0.5% are only for IM administration; products containing sodium chloride 0.9% can be administered via the IM or IV route.

Iron sucrose (Venofer): 20 mg/mL (20 mg elemental Fe/mL) (2.5, 5, 10 mL); contains 300 mg/mL sucrose; preservative free.

IRON—INJECTABLE PREPARATIONS *continued***Ferric gluconate (IV):**

**Iron-deficiency anemia in patients undergoing chronic hemodialysis who are receiving supplemental erythropoietin therapy (most require 8 doses at 8 sequential dialysis treatments to achieve a favorable response):**

**Child  $\geq 6$  yr:** 1.5 mg/kg elemental Fe (0.12 mL/kg) IV; **max. dose** 125 mg elemental Fe/dose.

Dilute dose in 25 mL NS and infuse over 1 hr.

**Adult:** 125 mg elemental Fe in 100 mL NS IV; infuse over 1 hr. Most require a minimal cumulative dose of 1 g elemental Fe administered over 8 sessions.

**Iron dextran (IV or IM):****Iron-deficiency anemia:**

**Test dose:** 25 mg (12.5 mg for infants) IV (over 5 min) or IM. May initiate treatment dose 1 hr after test dose.

Total replacement dose of iron dextran (mL) =  $0.0476 \times \text{Lean body wt (kg)} \times (\text{Desired Hb [g/dL]} - \text{Measured Hb [g/dL]}) + 1 \text{ mL per } 5 \text{ kg lean body weight (up to max. of } 14 \text{ mL)}$ .

**Acute blood loss:** Total replacement dose of iron dextran (mL) =  $0.02 \times \text{Blood loss (mL)} \times \text{Hematocrit expressed as decimal fraction}$ . Assumes 1 mL of RBC = 1 mg elemental iron. If no reaction to test dose, give remainder of replacement dose  $\div$  over 2–3 daily doses.

**Max daily (IM) dose:**

**<5 kg:** 0.5 mL (25 mg)

**5–10 kg:** 1 mL (50 mg)

**>10 kg:** 2 mL (100 mg)

**IM administration:** Use "Z-track" technique.

**IV administration:** Dilute in NS at a **max. concentration** of 50 mg/mL and infuse over 1–6 hr at a **max. rate** of 50 mg/min.

**Iron sucrose (IV):****Iron-deficiency anemia in patients with chronic kidney disease:**

**Child (limited data from 14 children with ESRD on hemodialysis):** 1 mg/kg/dialysis was adequate for correcting ferritin levels, and 0.3 mg/kg/dialysis was successful in maintaining ferritin levels between 193–250 mcg/L. Doses were administered during last hr of each dialysis; recommended frequency, 3 times a week. A 10-mg test dose was administered.

**Adult:**

**Hemodialysis dependent:** 100 mg elemental Fe 1–3 times a wk during dialysis up to a total cumulative dose of 1000 mg. May continue to administer at lowest dose to maintain target Hb, Hct, and iron levels.

**Non-hemodialysis dependent:** 200 mg elemental Fe on 5 different days over a 2-wk period (total cumulative dose: 1000 mg).

**IV administration:** May administer undiluted over 2–5 min. For an infusion, dilute each 100 mg with a **max.** of 100 mL NS and infuse over at least 15 min.

Oral therapy with iron salts is preferred; injectable routes are painful. Gluconate and sucrose salts may be better tolerated than iron dextran. Adverse effects include hypotension, GI disturbances, fever, rash, myalgia, arthralgias, cramps, and headaches. Hypersensitivity reactions (fatal anaphylaxis with iron dextran; use test dose before first therapeutic dose) have been reported.



**IM administration is only possible with iron dextran salt.** Follow infusion recommendations for specific product. Monitor vital signs during IV infusion. TIBC levels may not be meaningful within 3 wk after dosing.

Efficacy and safety of iron sucrose for maintenance therapy has been evaluated in children 2 yr and older with CKD and receiving erythropoietin therapy. Common side effects include headache, respiratory tract viral infection, peritonitis, vomiting, pyrexia, dizziness, and cough. Pregnancy category is "B" for ferric gluconate and iron sucrose and "C" for iron dextran.

**IRON—ORAL PREPARATIONS**

Fergon, Fer-In-Sol, Feosol, Niferex, Slow FE, and many generics

**Oral iron supplements**

No



No



2



A

**Ferrous sulfate (20% elemental Fe):**

Drops and oral solution (Fer-In-Sol and generics) [OTC]: 75 mg (15 mg Fe)/1 mL (50 mL); contains 0.2% alcohol and sodium bisulfite

Oral elixir and liquid [OTC]: 220 mg (44 mg Fe)/5 mL; may contain 5% alcohol

Oral syrup [OTC]: 300 mg (60 mg Fe)/5 mL

Tabs [OTC]: 300 mg (60 mg Fe), 324 mg (65 mg Fe), 325 mg (65 mg Fe)

Extended-release tabs (Slow FE and generics) [OTC]: 140 mg (45 mg Fe), 160 mg (50 mg Fe), and 325 mg (65 mg Fe)

**Ferrous gluconate (12% elemental Fe):**

Tabs (Fergon and generics) [OTC]: 240 mg (27 mg Fe), 256 mg (28 mg Fe), 325 mg (36 mg Fe)

**Ferrous fumarate (33% elemental Fe):**

Tabs [OTC]: 90 mg (29.5 mg Fe), (324 mg (106 mg Fe), 325 mg (106 mg Fe), 456 mg (150 mg Fe)

**Polysaccharide-iron complex and ferrous bis-glycinate chelate (Niferex and generics)****(expressed in mg elemental Fe):**

Caps [OTC]: 50, 150 mg; 150 mg strength may contain 50 mg vitamin C

Elixir [OTC]: 100 mg/5 mL (237 mL); contains 10% alcohol

**Iron-deficiency anemia:****Premature infant:** 2–4 mg elemental Fe/kg/24 hr ÷ once daily–BID PO; **max. dose** 15 mg elemental Fe/24 hr**Child:** 3–6 mg elemental Fe/kg/24 hr ÷ once daily–TID PO**Adult:** 60–100 mg elemental Fe BID PO up to 60 mg elemental Fe QID**Prophylaxis:****Child:** Give dose below PO ÷ once daily–TID.**Premature:** 2 mg elemental Fe/kg/24 hr; **max. dose** 15 mg elemental Fe/24 hr**Full term:** 1–2 mg elemental Fe/kg/24 hr; **max. dose** 15 mg elemental Fe/24 hr**Adult:** Give 60–100 mg elemental Fe/24 hr PO ÷ once daily–BID.**Contraindicated** in hemolytic anemia and hemochromatosis. **Avoid** use in GI tract inflammation.

Iron preparations are variably absorbed. Less GI irritation when given with or after meals.

Vitamin C, 200 mg per 30 mg iron, may enhance absorption. Liquid iron preparations may stain

teeth. Give with dropper or drink through straw. May produce constipation, dark stools (false-positive guaiac is controversial), nausea, and epigastric pain. Iron and tetracycline inhibit each other's absorption. Antacids may decrease iron absorption.

**ISONIAZID**

INH, Nydrazid, Laniazid, and generics

In combination with rifampin: Rifamate, IsonaRif

In combination with rifampin and pyrazinamide: Rifater

**Antituberculous agent**

Yes



Yes



1



C

**Tabs:** 100, 300 mg**Syrup:** 50 mg/5 mL (473 mL)**Injection:** 100 mg/mL (10 mL); contains 0.25% chlorobutanol**In combination with rifampin:**

Caps (Rifamate, IsonaRif): 150 mg isoniazid + 300 mg rifampin

**In combination with rifampin and pyrazinamide:**

Caps (Rifater): 50 mg isoniazid + 120 mg rifampin + 300 mg pyrazinamide

ISONIAZID *continued*

See most recent edition of the AAP *Red Book* for details and length of therapy.

**Prophylaxis:**

**Infant and child:** 10 mg/kg (**max. dose** 300 mg) PO once daily. After 1 mo of daily therapy and in cases where daily compliance cannot be assured, may change to 20–40 mg/kg (**max. dose** 900 mg) per dose PO, given twice weekly.

**Adult:** 300 mg PO once daily

**Treatment:****Infant and child:**

10–15 mg/kg (**max. dose** 300 mg) PO once daily or 20–30 mg/kg (**max. dose** 900 mg) per dose twice weekly with rifampin for uncomplicated pulmonary tuberculosis in compliant patients. Additional drugs are necessary in complicated disease.

**Adult:**

5 mg/kg (**max. dose** 300 mg) PO once daily or 15 mg/kg (**max. dose** 900 mg) per dose twice weekly with rifampin. Additional drugs are necessary in complicated disease.

**For INH-resistant TB:** Discuss with Health Department or consult ID specialist.

**Should not be used alone for treatment. Contraindicated** in acute liver disease and previous isoniazid-associated hepatitis. Peripheral neuropathy, optic neuritis, seizures, encephalopathy, psychosis, hepatic side effects may occur with higher doses, especially in combination with rifampin. Severe liver injury has been reported in children and adults treated for latent TB. Follow LFTs monthly. Supplemental pyridoxine (1–2 mg/kg/24 hr) is recommended. May cause false-positive urine glucose test.

Inhibits CYP 450 1A2, 2C9, 2C19, and 3A3/4 microsomal enzymes; decrease dose of carbamazepine, diazepam, phenytoin, and prednisone. Prednisone may decrease isoniazid's effects. Also a substrate and inducer of CYP 450 2E1 and may potentiate acetaminophen hepatotoxicity. Avoid daily alcohol use to reduce risk for isoniazid-induced hepatitis.

May be given IM (same as oral doses) when oral therapy is not possible. Administer oral doses 1 hr before and 2 hr after meals. Aluminum salts may decrease absorption.

**ISOPROTERENOL**

Isuprel

**Adrenergic agonist**



No



Yes



?



C

**Injection:** 0.2 mg/mL (5, 10 mL); contains sulfites

**NOTE:** Dosage units for adults are in mcg/min, compared with mcg/kg/min for children.

**IV infusion:**

**Neonate-child:** 0.05–2 mcg/kg/min; start at minimal dose and increase every 5–10 min by 0.1 mcg/kg/min until desired effect or onset of toxicity; **max. dose** 2 mcg/kg/min.

**Adult:** 2–20 mcg/min; titrate to desired effect.

**Use with caution** in diabetes, hyperthyroidism, renal disease, CHF, ischemia, or aortic stenosis. May cause flushing, ventricular arrhythmias, profound hypotension, anxiety, and myocardial ischemia. Monitor heart rate, respiratory rate, and blood pressure. **Not** for treatment of asystole or for use in cardiac arrests unless bradycardia is due to heart block.

Continuous infusion for bronchodilation must be gradually tapered over a 24–48 hr period to prevent rebound bronchospasm. Tolerance may occur with prolonged use. Clinical deterioration, myocardial necrosis, CHF, and **death** have been reported with continuous infusion use in refractory asthmatic children.

**ISOTRETINOIN**

Accutane, Absorica, Amnesteem, Claravis, Myorisan, Zenatane

**Retinoic acid, vitamin A derivative**

Yes



No



3



X

**Caps:** 10, 20, 30, 40 mg; may contain soybean oil, EDTA, and parabens**Cystic acne:**

**Child (>12 yr) and adult:** 0.5–2 mg/kg/24 hr ÷ BID PO × 15–20 wk or until total cyst count decreases by 70%, whichever comes first. Dosages as low as 0.05 mg/kg/24 hr have been reported to be beneficial.

**Contraindicated during pregnancy; known teratogen. Use with caution** in females during childbearing years. May cause conjunctivitis, xerosis, pruritus, photosensitivity reactions (avoid exposure to sunlight and use sunscreen), epistaxis, anemia, hyperlipidemia, pseudotumor cerebri (especially in combination with tetracyclines; avoid this combination), cheilitis, bone pain, muscle aches, skeletal changes, lethargy, nausea, vomiting, elevated ESR, mental depression, aggressive/violent behavior, and psychosis. Serious skin reactions (e.g., Stevens-Johnson syndrome, TEN) have been reported.

Elevation of liver enzymes may occur during treatment; a dosage reduction or continued treatment may result in normalization. Discontinue use if liver enzymes do not normalize or if hepatitis is suspected.

To avoid additive toxic effects, **do not** take vitamin A concomitantly. Increases clearance of carbamazepine. Hormonal birth control (oral, injectable, and implantable) failures have been reported with concurrent use. Monitor CBC, ESR, triglycerides, and LFTs.

Prescribers, site pharmacists, patients, and wholesalers must register with the iPLEDGE system (a risk minimization program) at [www.ipledeprogram.com](http://www.ipledeprogram.com) or 1-866-495-0654 before doses are dispensed. Prescriptions may not be written for more than a 1-mo supply.

**ITRACONAZOLE**

Sporanox, Onmel, and generics

**Antifungal agent**

Yes



Yes



3



C

**Caps** (Sporanox and generics): 100 mg**Tab**s (Onmel): 200 mg**Oral solution** (Sporanox): 10 mg/mL (150 mL); contains saccharin and sorbitol

**Neonate (limited data in full-term neonates treated for tinea capitis):** 5 mg/kg/24 hr PO once daily × 6 wk

**Child (limited data):** 3–5 mg/kg/24 hr PO ÷ once daily–BID; dosages as high as 5–10 mg/kg/24 hr have been used for *Aspergillus* prophylaxis in chronic granulomatous disease. Population pharmacokinetic data in pediatric cystic fibrosis and bone marrow transplant patients suggest an oral liquid dosage of 10 mg/kg/24 hr PO ÷ BID **OR** oral capsule dosage of 20 mg/kg/24 hr PO ÷ BID to be more reliable for achieving trough plasma levels between 500 and 2000 ng/mL.

**Prophylaxis for recurrence of opportunistic disease in HIV:**

**Coccidioides spp.:** 2–5 mg/kg/dose PO Q12 hr; **max. dose** 400 mg/24 hr

**Cryptococcus neoformans:** 5 mg/kg/dose PO Q24 hr; **max. dose** 200 mg/24 hr

**Histoplasma capsulatum:** 5 mg/kg/dose PO Q12 hr; **max. dose** 400 mg/24 hr

**Treatment of opportunistic disease in HIV:**

**Candidiasis:** 5 mg/kg/24 hr PO ÷ Q12–24 hr; **max. dose** 400 mg/24 hr

**Coccidioides spp.:** 5–10 mg/kg/dose PO BID × 3 days, followed by 2–5 mg/kg/dose PO BID; **max. dose** 400 mg/24 hr

ITRACONAZOLE *continued***Treatment of opportunistic disease in HIV (cont.):**

**Cryptococcus neoformans:** 2.5–5 mg/kg/dose (**max. dose** 200 mg/dose) PO TID × 3 days, followed by 5–10 mg/kg/24 hr (**max. dose** 400 mg/24 hr) ÷ once to twice daily for a minimum of 8 wk

**Histoplasma capsulatum:** 2–5 mg/kg/dose (**max. dose** 200 mg/dose) PO TID × 3 days, followed by 2–5 mg/kg/dose (**max. dose** 200 mg/dose) PO BID × 12 mo

**Adult:**

**Blastomycosis and nonmeningeal histoplasmosis:** 200 mg PO once daily up to a **max. dose** of 400 mg/24 hr ÷ BID (**max. dose** 200 mg/dose)

**Aspergillosis and severe infections:** 600 mg/24 hr PO ÷ TID × 3–4 days, followed by 200–400 mg/24 hr ÷ BID; **max. dose** 600 mg/24 hr ÷ TID

Oral solution and capsule dosage form should **NOT** be used interchangeably; oral solution is more bioavailable. Only the oral solution has been demonstrated effective for oral and/or esophageal candidiasis. **Contraindicated** in CHF and certain interacting drugs (see below). **Use with caution** in hepatic and/or renal impairment, cardiac dysrhythmias, and azole hypersensitivity. May cause GI symptoms, headaches, rash, liver enzyme elevation, hepatitis, and hypokalemia.

Like ketoconazole, it inhibits activity of CYP 450 3A4 drug metabolizing isoenzyme. Thus, coadministration of cisapride, dofetilide, felodipine, methadone, nisoldipine, pimozide, quinidine, triazolam, lovastatin, simvastatin, ergot derivatives, and oral midazolam is **contraindicated**. See remarks at *Ketoconazole* for additional drug interaction information.

Steady-state trough serum concentrations of >250 ng/mL itraconazole and >1000 ng/mL hydroxyitraconazole (metabolite) have been recommended. Recommended serum sampling time at steady state: trough level after 2 wk of continuous dosing.

Administer oral solution on an empty stomach, but administer capsules with food. Achlorhydria reduces absorption of drug. **Do not** use oral liquid dosage form in patients with GFR <30 mL/min; the hydroxypropyl-β-cyclodextrin excipient has reduced clearance with renal failure.

**KANAMYCIN**

Kantrex and generics

**Antibiotic, aminoglycoside**

No



Yes



2



D

**Injection:** 333 mg/mL (3 mL); may contain sulfites

**Neonate IV/IM administration (see following table):**

Birth Weight (kg)	<7 days	≥7 days
<2	15 mg/kg/24 hr ÷ Q12 hr	22.5 mg/kg/24 hr ÷ Q8 hr
≥2	20 mg/kg/24 hr ÷ Q12 hr	30 mg/kg/24 hr ÷ Q8 hr

**Infant and child:** IM/IV: 15–30 mg/kg/24 hr ÷ Q8–12 hr

**Adult:** IV/IM: 15 mg/kg/24 hr ÷ Q8–12 hr

**PO administration for GI bacterial overgrowth:** 150–250 mg/kg/24 hr ÷ Q6 hr; **max. dose** 4 g/24 hr

Renal toxicity and ototoxicity may occur. Give over 30 min if IV route is used. Use with caution in neuromuscular disorders (e.g., infant botulism, myasthenia gravis), anesthesia and muscle-relaxant medications, and hypermagnesemia (may result in respiratory arrest). **Adjust dose in renal failure (see Chapter 31).** Poorly absorbed orally; PO used to treat GI bacterial overgrowth. Oral route is **contraindicated** in intestinal obstructions. **Avoid** use with loop diuretics.

Therapeutic levels: Peak, 15–30 mg/L; trough, <5–10 mg/L. Recommended serum sampling time at steady state: trough within 30 min before third consecutive dose, and peak 30–60 min after administration of third consecutive dose.



**KETAMINE**

Ketalar and various generics

**General anesthetic**

No



No



3



B

**Injection:** 10 mg/mL (20 mL), 50 mg/mL (10 mL), 100 mg/mL (5, 10 mL); contains benzethonium chloride**Child (see remarks):****Sedation:****PO:** 5 mg/kg  $\times$  1**IV:** 0.25–1 mg/kg**IM:** 2–5 mg/kg  $\times$  1**Adult:****Analgesia with sedation:**

IV (see remarks): 0.2–1 mg/kg

IM: 0.5–4 mg/kg



**Contraindicated** in elevated ICP, hypertension, aneurysms, thyrotoxicosis, CHF, angina, and psychotic disorders. May cause hypertension, hypotension, emergence reactions, tachycardia, laryngospasm, respiratory depression, and stimulation of salivary secretions. Cystitis has been reported with chronic use/abuse. IV use may induce general anesthesia. Coadministration of an anticholinergic agent may be added in situations of clinically significant hypersalivation in patients with impaired ability to mobilize secretions. Benzodiazepine may be used in the presence of a ketamine-associated recovery reaction (prophylaxis use in adults may be beneficial). Ondansetron prophylaxis can slightly reduce vomiting. See *Ann Emerg Med.* 2001;57:449-461 for additional use information in the emergency department.

Rate of IV infusion should **not** exceed 0.5 mg/kg/min and should **not** be administered in <60 sec. For additional information, including onset and duration of action, see Chapter 6.

Pregnancy category is considered by many as a "B" despite no formal designation by the FDA.

**KETOCONAZOLE**

Nizoral, Nizoral A-D, Xolegel, Extina, and generics

**Antifungal agent, imidazole**

Yes



No



2



C

**Tabs:** 200 mg**Oral suspension:** 100 mg/5 mL **Cream:** 2% (15, 30, 60 g); contains sulfites**Gel:** 2% [Xolegel] (45 g); contains 34% alcohol**Shampoo:** 1% [Nizoral A-D, OTC] (120, 210 mL), 2% (120 mL)**Foam:** 2% [Extina] (50, 100 g)**Oral:****Child  $\geq$  2 yr:** 3.3–6.6 mg/kg/24 hr once daily**Adult:** 200–400 mg/24 hr once daily**Max. dose:** 800 mg/24 hr  $\div$  BID**Topical:** 1–2 applications/24 hr**Shampoo (dandruff):** Twice weekly, with at least 3 days between applications for up to 8 weeks PRN.

Thereafter, intermittently as needed to maintain control.

**Suppressive therapy against mucocutaneous candidiasis in HIV:****Child:** 5–10 mg/kg/24 hr  $\div$  once daily–BID PO; **max. dose** of 800 mg/24 hr  $\div$  BID**Adolescent and adult:** 200 mg/dose once daily PO

The systemic dosage form should not be first-line treatment for any fungal infection, owing to concerns of hepatotoxicity and adrenal gland effects (per FDA).



KETOCONAZOLE *continued*

Monitor LFTs in long-term use and adrenal function for patients at risk. Drugs that decrease gastric acidity will decrease absorption. May cause nausea, vomiting, rash, headache, pruritus, and fever.

Hepatotoxicity (including fatal cases) has been reported; use with hepatic impairment is **contraindicated**. High doses may decrease adrenocortical function and serum testosterone levels.

Hypersensitivity reactions (including anaphylaxis) have been reported with all dosage forms.

Safety and efficacy with topical use in seborrheic dermatitis for patients >age 12 yr has been established. Avoid topical use on breast or nipples in nursing mothers.

Inhibits CYP 450 3A4. **Contraindicated** when used with cisapride, mefloquine, quinidine, terfenadine, pimozide, any drug that can prolong QT interval (risk for cardiac arrhythmias), and HMG-CoA reductase inhibitors (e.g., simvastatin, lovastatin). Excessive sedation and prolonged hypnotic effects with triazolam use (also **contraindicated**). May increase levels/effects of phenytoin, digoxin, cyclosporine, corticosteroids, nevirapine, protease inhibitors, and warfarin. Achlorhydria, phenobarbital, rifampin, isoniazid, H<sub>2</sub> blockers, antacids, and omeprazole can decrease levels of oral ketoconazole.

Administering oral doses with food or acidic beverages and 2 hr before antacids will increase absorption.

To use shampoo, wet hair and scalp with water, apply sufficient amount to scalp, and gently massage for about 1 min. Rinse hair thoroughly, reapply shampoo, leave on scalp for an additional 3 min, then rinse.

**KETOROLAC**

Many generics (previously available as Toradol), Acular,  
Acular LS, Acuvail

**Nonsteroidal anti-inflammatory agent**



Yes



Yes



2



C/D

**Injection:** 15 mg/mL (1 mL), 30 mg/mL (1, 2, 10 mL); contains 10% alcohol and tromethamine

**Tabs:** 10 mg; contains tromethamine

**Ophthalmic solution (all contain tromethamine):**

Acular: 0.5% (5, 10 mL); contains benzalkonium chloride

Acular LS and generics: 0.4% (3, 5, 10 mL); contains benzalkonium chloride

Acuvail: 0.45% (0.4 mL; 30s); preservative free

**Systemic use is not to exceed 3–5 days; regardless of administration route (IM, IV, PO).**

**IM/IV:**

**Child:** 0.5 mg/kg/dose IM/IV Q6–8 hr. **Max. dose:** 30 mg Q6 hr or 120 mg/24 hr. Alternatively, manufacturer has recommended following doses for children aged 2–16 yr with moderate/severe acute pain:

**IV:** 0.5 mg/kg × 1; **max. dose** 15 mg

**IM:** 1 mg/kg × 1; **max. dose** 30 mg

**Adult:** 30 mg IM/IV Q6 hr; **max. dose:** 120 mg/24 hr

**PO:**

**Child > 16 yr (>50 kg) and adult:** 10 mg PRN Q6 hr; **max. dose** 40 mg/24 hr

**Ophthalmic (see remarks):**

**≥3 yr–adult:** 1 drop in each affected eye QID

May cause GI bleeding, nausea, dyspepsia, drowsiness, decreased platelet function, and interstitial nephritis. **Not recommended** in patients at increased risk of bleeding.

**Do not use** in hepatic or renal failure. **Use with caution** in heart disease (risk for MI and stroke with prolonged use).

Duration of therapy for ophthalmic use: 14 days after cataract surgery, and up to 4 days after corneal refractive surgery. Also indicated for ocular itching associated with seasonal allergic conjunctivitis.

Bronchospasm or asthma exacerbations have been reported with ophthalmic use.

Pregnancy category changes to a "D" if used in the third trimester.



**LABETALOL**

Normodyne, Trandate, and various generics

**Adrenergic antagonist ( $\alpha$  and  $\beta$ ), antihypertensive**

Yes



No



2



C/D

**Tab:** 100, 200, 300 mg**Injection:** 5 mg/mL (4, 20, 40 mL); contains parabens**Oral suspension:** 10, 40 mg/mL **Child (see remarks):****PO:** Initial: 1–3 mg/kg/24 hr ÷ BID. May increase up to a maximum of 12 mg/kg/24 hr up to 1200 mg/24 hr.**IV:** Hypertensive emergency (start at lowest dose and titrate to effect; see Chapter 4 for additional information):**Intermittent dose:** 0.2–1 mg/kg/dose Q10 min PRN; **max. dose** 40 mg/dose.**Infusion (hypertensive emergencies):** 0.4–1 mg/kg/hr to a **max. dose** of 3 mg/kg/hr. May initiate with a 0.2–1 mg/kg bolus; **max. bolus** 40 mg.**Adult (see remarks):****PO:** 100 mg BID; increase by 100 mg/dose Q2–3 days PRN to a **max. dose** of 2.4 g/24 hr. Usual range: 200–800 mg/24hr ÷ BID.**IV:** Hypertensive emergency (start at lowest dose and titrate to effect, with a **max. total dose** of 300 mg for both methods of administration):**Intermittent dose:** 20–80 mg/dose (begin with 20 mg) Q10 min PRN**Infusion:** 2 mg/min, increase to titrate to response**Contraindicated** in asthma, pulmonary edema, cardiogenic shock, and heart block. May cause orthostatic hypotension, edema, CHF, bradycardia, AV conduction disturbances, bronchospasm, urinary retention, and skin tingling. **Use with caution** in hepatic disease (dose reduction may be necessary), diabetes, liver function test elevation, hepatic necrosis, and hepatitis. Cholestatic jaundice have been reported. Use with digitalis glycosides may increase risk for bradycardia.

Patient should remain supine for up to 3 hr after IV administration. Pregnancy category changes to "D" if used in second or third trimesters.

Onset of action: PO: 1–4 hr; IV: 5–15 min.

**LACOSAMIDE**

Vimpat

**Anticonvulsant**

Yes



Yes



?



C

**Oral solution:** 10 mg/mL (200, 465 mL); contains aspartame and propylene glycol**Tab:** 50, 100, 200 mg**Injection:** 10 mg/mL (20 mL)**Child (3–18 yr; limited data in 18 patients with refractory partial seizures as adjunctive therapy with moderate response):** Start at 1 mg/kg/24 hr PO ÷ BID. If needed, dose may be increased at weekly intervals by 1 mg/kg/24 hr, administered BID up to 10 mg/kg/24 hr. The final doses ranged from 2–10 mg/kg/24 hr. A retrospective trial in 16 patients 8–21 years old with focal seizures as adjunctive therapy received an average dose of 4.7 mg/kg/24 hr PO with moderate response.**A randomized placebo-controlled trial for lacosamide as an add-on therapy for patients 4–<17 yr with partial-onset seizures is evaluating the following dosages (see [www.clinicaltrials.gov](http://www.clinicaltrials.gov) for updates):**

&lt;30 kg: 8–12 mg/kg/24 hr PO ÷ BID

≥30–&lt;50 kg: 6–8 mg/kg/24 hr PO ÷ BID

≥50 kg: 150–200 mg PO BID

LACOSAMIDE *continued***≥17 yr and adult:**

**Partial-onset seizures:** Start at 50 mg BID IV/PO. If needed, dose may be increased at weekly intervals by 100 mg/24 hr, administered BID up to the usual maintenance dose of 200–400 mg/24 hr ÷ BID. Use same dose when converting from IV to PO and vice versa. IV use should be considered for temporary use.

**Use with caution** with known cardiac conduction problems (e.g., second-degree AV block), severe cardiac disease (e.g., MI or heart failure), concomitant use with drugs known to prolong PR interval, and renal (see Chapter 31) and hepatic impairment. In adults with GFR < 30 mL/min and ESRD, the maximum daily dosage is 300 mg/24 hr. Lacosamide is 95% excreted by the kidneys. Dose reduction may be necessary with hepatic or renal impairment and concurrent strong inhibitor of CYP 450 3A4 or 2C9 medication. Use is **not recommended** in severe hepatic impairment, and an adult **max. dose** of 300 mg/24 hr is recommended for mild/moderate hepatic impairment. Oral bioavailability is ≈ 100%.

Most common side effects in adults include diplopia, headache, dizziness, and nausea. Somnolence and irritability were frequently reported in pediatric studies. Patients should be advised of potential dizziness, ataxia, and syncope with use. Multiorgan hypersensitivity reactions (affecting skin, kidney, liver) and euphoria (high doses) have been reported. As with other AEDs, monitor for suicidal behavior and ideation.

Oral doses may be administered with or without food. IV doses should be administered over 30–60 min. **Do not** abruptly withdraw therapy; gradually taper to prevent potential seizures.

**LACTULOSE**

Cephulac, Chronulac, Enuloase, Kristalose, and generics

**Ammonium detoxicant, hyperosmotic laxative**



No



No



?



B

**Syrup:** 10 g/15 mL (15, 30, 237, 473, 960, 1893 mL); contains galactose, lactose, and other sugars

**Crystals for reconstitution (Kristalose):** 10 g (30s), 20 g (30s)

**Constipation:**

**Child:** 1–3 mL/kg/24 hr PO ÷ BID; **max. dose** 60 mL/24 hr

**Adult:** 15–30 mL/24 hr PO once daily to a **max. dose** of 60 mL/24 hr

**Portal systemic encephalopathy (adjust dose to produce 2–3 soft stools/day):**

**Infant:** 2.5–10 mL/24 hr PO ÷ TID–QID

**Child:** 40–90 mL/24 hr PO ÷ TID–QID

**Adult:** 30–45 mL/dose PO TID–QID; acute episodes, 30–45 mL Q1–2 hr until 2–3 soft stools/day

**Rectal (adult):** 300 mL diluted in 700 mL water or NS in 30–60 min retention enema; may give Q4–6 hr

**Contraindicated** in galactosemia. **Use with caution** in diabetes mellitus. GI discomfort and diarrhea may occur. For portal systemic encephalopathy, monitor serum ammonia, serum potassium, and fluid status.

Adjust dose to achieve 2–3 soft stools per day. **Do not use** with antacids. Dissolve crystal dosage form with 4 ounces of water or juice. All doses may be administered with juice, milk, or water.

**LAMIVUDINE**

Epivir, Epivir-HBV, 3TC, and generics

**Antiviral agent, nucleoside analog reverse transcriptase inhibitor**

Yes



Yes



3



C

**Tabs:** 100 mg (Epivir-HBV), 150, 300 mg**Oral solution:** 5 mg/mL (Epivir-HBV) (240 mL), 10 mg/mL (Epivir) (240 mL); contains parabensHIV: See [www.aidsinfo.nih.gov/guidelines](http://www.aidsinfo.nih.gov/guidelines).**Prevention of maternal-fetal transmission to reduce nevirapine resistance (for infants born to mothers with no antiretroviral therapy before or during labor, infants born to mothers with only intrapartum antiretroviral therapy, infants born to mothers with suboptimal viral suppression at delivery, or infants born to mothers with known antiretroviral drug resistance):****Neonate:** 2 mg/kg/dose PO BID  $\times$  7–14 days from birth**Chronic hepatitis B (see remarks):****2–17 yr:** 3 mg/kg/dose PO once daily up to a **max. dose** of 100 mg/dose **$\geq 18$  and adult:** 100 mg/dose PO once dailySee [aidsinfo.nih.gov/guidelines](http://aidsinfo.nih.gov/guidelines) for remarks for use in HIV.

May cause headache, fatigue, GI disturbances, rash, and myalgia/arthralgia. Lactic acidosis, severe hepatomegaly with steatosis, posttreatment exacerbations of hepatitis B and ALT elevations, pancreatitis, and emergence of resistant viral strains have been reported. Concomitant use with cotrimoxazole (TMP/SMX) may result in increased lamivudine levels.

**Use Epivir-HBV product for chronic hepatitis B indication.** Safety and effectiveness beyond 1 yr have not been determined. Patients with both HIV and hepatitis B should use the higher HIV doses along with an appropriate combination regimen.May be administered with food. **Adjust dose in renal impairment (see Chapter 31).****LAMOTRIGINE**

Lamictal, Lamictal ODT, Lamictal XR, and generics

**Anticonvulsant**

Yes



Yes



2



C

**Tabs:** 25, 100, 150, 200 mg**Extended-release tabs (Lamictal XR and generics):** 25, 50, 100, 200, 250, 300 mg**Chewable tabs:** 2, 5, 25 mg**Orally disintegrated tabs (Lamictal ODT):** 25, 50, 100, 200 mg**Oral suspension:** 1 mg/mL **Child 2–12 yr, adjunctive therapy (see remarks):****WITH antiepileptic drugs (AEDs) other than carbamazepine, phenytoin, phenobarbital, primidone, or valproic acid (use immediate-release dosage forms):****Wk 1 and 2:** 0.3 mg/kg/24 hr PO  $\div$  once daily–BID, rounded down to the nearest whole tablet**Wk 3 and 4:** 0.6 mg/kg/24 hr PO  $\div$  BID, rounded down to the nearest whole tablet**Usual maintenance dose:** 4.5–7.5 mg/kg/24 hr PO  $\div$  BID, titrated to effect. To achieve the usual maintenance dose, increase doses Q1–2 wk by 0.6 mg/kg/24 hr (rounded down to the nearest whole tablet) as needed.**Max. dose:** 300 mg/24 hr  $\div$  BID**WITH enzyme-inducing AEDs WITHOUT valproic acid (use immediate-release dosage forms):****Wk 1 and 2:** 0.6 mg/kg/24 hr PO  $\div$  BID, rounded down to the nearest whole tablet**Wk 3 and 4:** 1.2 mg/kg/24 hr PO  $\div$  BID, rounded down to the nearest whole tablet

LAMOTRIGINE *continued*

**Usual maintenance dose:** 5–15 mg/kg/24 hr PO ÷ BID, titrated to effect. To achieve the usual maintenance dose, increase doses Q1–2 wk by 1.2 mg/kg/24 hr (rounded down to the nearest whole tablet) as needed.

**Max. dose:** 400 mg/24 hr ÷ BID

**WITH AEDs WITH valproic acid (use immediate-release dosage forms):**

**Wk 1 and 2:** 0.15 mg/kg/24 hr PO ÷ once daily–BID, rounded down to the nearest whole tablet (see following table)

**Wk 3 and 4:** 0.3 mg/kg/24 hr PO ÷ once daily–BID, rounded down to the nearest whole tablet (see following table)

Weight (kg)	Weeks 1 & 2	Weeks 3 & 4
6.7–14	2 mg every other day	2 mg once daily
14.1–27	2 mg once daily	4 mg/24 hr ÷ once daily–BID
27.1–34	4 mg/24 hr ÷ once daily–BID	8 mg/24 hr ÷ once daily–BID
34.1–40	5 mg once daily	10 mg/24 hr ÷ once daily–BID

**Usual maintenance dose:** 1–5 mg/kg/24 hr PO ÷ once daily–BID, titrated to effect. To achieve the usual maintenance dose, increase doses Q1–2 wk by 0.3 mg/kg/24 hr (rounded down to the nearest whole tablet) as needed. If adding lamotrigine with valproic acid alone, usual maintenance dose is 1–3 mg/kg/24 hr.

**Max. dose:** 200 mg/24 hr

**>12 yr and adult adjunctive therapy:****WITH AEDs other than carbamazepine, phenytoin, phenobarbital, primidone, or valproic acid (use immediate-release dosage forms):**

**Wk 1 and 2:** 25 mg once daily PO

**Wk 3 and 4:** 50 mg once daily PO

**Usual maintenance dose:** 225–375 mg/24 hr ÷ BID PO, titrated to effect. To achieve the usual maintenance dose, increase doses Q1–2 wk by 50 mg/24 hr as needed.

**WITH enzyme-inducing AEDs WITHOUT valproic acid (use immediate-release dosage forms):**

**Wk 1 and 2:** 50 mg once daily PO

**Wk 3 and 4:** 50 mg BID PO

**Usual maintenance dose:** 300–500 mg/24 hr ÷ BID PO, titrated to effect. To achieve the usual maintenance dose, increase doses Q1–2 wk by 100 mg/24 hr as needed. Doses as high as 700 mg/24 hr ÷ BID have been used.

**WITH AEDs WITH valproic acid: (use immediate-release dosage forms):**

**Wk 1 and 2:** 25 mg every other day PO

**Wk 3 and 4:** 25 mg once daily PO

**Usual maintenance dose:** 100–400 mg/24 hr ÷ once daily–BID PO, titrated to effect. To achieve the usual maintenance dose, increase doses Q1–2 wk by 25–50 mg/24 hr as needed. If adding lamotrigine to valproic acid alone, usual maintenance dose is 100–200 mg/24 hr.

**Extended-release dosage form (Lamictal XR)**

**≥13 yr and adult adjunctive therapy (max. dose: increases after week 8: 100 mg/24 hr at weekly intervals; see remarks):**

	Weeks 1 & 2	Weeks 3 & 4	Week 5	Week 6	Week 7	Maintenance Dose
Patient NOT receiving enzyme-inducing drugs (e.g., carbamazepine) OR valproic acid	25 mg once daily	50 mg once daily	100 mg once daily	150 mg once daily	200 mg once daily	300–400 mg once daily

Continued

LAMOTRIGINE *continued*

	Weeks 1 & 2	Weeks 3 & 4	Week 5	Week 6	Week 7	Maintenance Dose
Patients receiving enzyme-inducing drugs (e.g., carbamazepine) WITHOUT valproic acid	50 mg once daily	100 mg once daily	200 mg once daily	300 mg once daily	400 mg once daily	400–600 mg once daily
Patients receiving valproic acid	25 mg every other day	25 mg once daily	50 mg once daily	100 mg once daily	150 mg once daily	200–250 mg once daily

**Converting from a single enzyme-inducing AED to lamotrigine monotherapy for child  $\geq 16$  yr and adult (titrate lamotrigine to maintenance dose; then gradually withdraw enzyme-inducing AED by 20% decrements over a 4-wk period; use immediate-release dosage forms):**

**Wk 1 and 2:** 50 mg once daily PO

**Wk 3 and 4:** 50 mg BID PO

**Usual maintenance dose:** 500 mg/24 hr  $\div$  BID PO, titrated to effect. To achieve the usual maintenance dose, increase doses Q1–2 wk by 100 mg/24 hr as needed.

**Bipolar disease (use immediate-release dosage forms):**

**$\geq 18$  yr and adult (PO; see table below):**

	Weeks 1 & 2	Weeks 3 & 4	Week 5	Week 6 and Thereafter
Patient NOT receiving enzyme-inducing drugs (e.g., carbamazepine) OR valproic acid	25 mg/24 hr	50 mg/24 hr	100 mg/24 hr	200 mg/24 hr (target dose)
Patients receiving enzyme-inducing drugs (e.g., carbamazepine) WITHOUT valproic acid	50 mg/24 hr	100 mg/24 hr $\div$ once daily–BID	200 mg/24 hr PO $\div$ once daily–BID	Week 6: 300 mg/24 hr $\div$ once daily–BID Week 7 and thereafter: may increase to 400 mg/24 hr $\div$ once daily–BID (target dose)*
Patients receiving valproic acid	25 mg every other day	25 mg/24 hr	50 mg/24 hr PO	100 mg/24 hr (target dose)†

\*If carbamazepine or other enzyme-inducing drug is discontinued, maintain current lamotrigine dose for 1 week, then decrease daily lamotrigine dose in 100-mg increments at weekly intervals until 200 mg/24 hr.

†If valproic acid is discontinued, increase by 50-mg weekly intervals up to 200 mg/24 hr.

Enzyme-inducing AEDs include carbamazepine, phenytoin, and phenobarbital. Stevens-Johnson syndrome, toxic epidermal necrolysis, and other potentially life-threatening rashes have been reported in children (0.8%) and adults (0.3%) for adjunctive therapy in seizures. Reported rates for adults treated for bipolar/mood disorders as monotherapy and adjunctive therapy are 0.08% and 0.13%, respectively. May cause fatigue, drowsiness, ataxia, rash (especially with valproic acid), headache, nausea, vomiting, and abdominal pain. Diplopia, nystagmus, aseptic meningitis, and alopecia have also been reported. Use during the first 3 mo of pregnancy may result in a higher chance for cleft lip or cleft palate in the newborn. Suicidal behavior or ideation have been reported.

If converting from immediate-release to extended-release dosage form, initial dose of extended-release drug should match total daily dose of immediate-release drug and be administered once daily. Adjust dose as needed with recommended dosage guidelines.



LAMOTRIGINE *continued*

Reduce maintenance dose in renal failure. Reduce all doses (initial, escalation, and maintenance) in liver dysfunction defined by Child-Pugh grading system as follows:

*Grade B:* Moderate dysfunction, decrease dose by  $\approx 50\%$

*Grade C:* Severe dysfunction, decrease dose by  $\approx 75\%$

Withdrawal symptoms may occur if discontinued suddenly. A stepwise dose reduction over  $\geq 2$  wk ( $\approx 50\%$  per week) is recommended unless safety concerns require a more rapid withdrawal.

Acetaminophen, carbamazepine, oral contraceptives (ethinylestradiol), phenobarbital, primidone, phenytoin, and rifampin may decrease levels of lamotrigine. Valproic acid may increase levels.

**LANSOPRAZOLE**

Prevacid, Prevacid SoluTab, First-Lansoprazole, and generics

**Gastric acid pump inhibitor**



Yes



No



?



B

**Caps, delayed-release:** 15, 30 mg

**Tabs, disintegrating delayed-release (Prevacid SoluTab):** 15, 30 mg; contains aspartame

**Granules for delayed-release oral suspension:** 15, 30 mg packets (30s)

**Oral suspension (First-Lansoprazole):** 3 mg/mL (90, 150, 300 mL); contains benzyl alcohol

**1–11 yr (short-term treatment of GERD and erosive esophagitis, for up to 12 wk):**

**Initial dose:**

$\leq 30$  kg: 15 mg PO once daily

$>30$  kg: 30 mg PO once daily–BID

**Subsequent dosage increase (if needed):** May be increased up to 30 mg PO BID after  $\geq 2$  wk of therapy without response at initial dose level.

**12 yr–adult:**

**GERD:** 15 mg PO once daily for up to 8 wk

**Erosive esophagitis:** 30 mg PO once daily  $\times$  8–16 wk; **maintenance dose:** 15 mg PO once daily

**Duodenal ulcer:** 15 mg PO once daily  $\times$  4 wk; **maintenance dose:** 15 mg PO once daily

**Gastric ulcer and NSAID-induced ulcer:** 30 mg PO once daily for up to 8 wk

**Hypersecretory conditions:** 60 mg PO once daily; dosage may be increased up to 90 mg PO BID, where doses  $>120$  mg/24 hr are divided BID.

Common side effects include GI discomfort, headache, fatigue, rash, and taste perversion.

Microscopic colitis resulting in watery diarrhea has been reported, and switching to an alternative proton pump inhibitor may be beneficial in resolving diarrhea.

Drug is a substrate for CYP 450 2C19 and 3A3/4. May decrease absorption of itraconazole, ketoconazole, iron salts, and ampicillin esters; may increase levels/effects of methotrexate, tacrolimus, and warfarin. Theophylline clearance may be enhanced. **Reduce dose in severe hepatic impairment.** May be used in combination with clarithromycin and amoxicillin for *Helicobacter pylori* infections.

In a multicenter double-blind parallel-group study in infants (1 mo–1 yr) with GERD, lansoprazole was no more effective than placebo.

Administer all oral doses before meals and 30 min before sucralfate. **Do not** crush or chew granules (all dosage forms). Capsule may be opened and intact granules administered in an acidic beverage or food (e.g., apple or cranberry juice, applesauce). **Do not** break or cut orally disintegrating tablets. Use of oral disintegrating tablets dissolved in water has been reported to clog and block oral syringes and feeding tubes (gastric and jejunostomy). For IV use, use a 1.2- micron inline filter.



**LEVALBUTEROL**

Xopenex, Xopenex HFA, and generics

 ***$\beta_2$ -Adrenergic agonist***

No



No



1



C

**Prediluted nebulized solution:** 0.31 mg in 3 mL, 0.63 mg in 3 mL, 1.25 mg in 3 mL (30s)**Concentrated nebulized solution:** 1.25 mg/0.5 mL (0.5 mL) (30s)**Aerosol inhaler (MDI; Xopenex HFA):** 45 mcg/actuation (15 g delivers 200 doses)***Nebulizer:*****≤4 yr:** Start at 0.31 mg inhaled Q4–6 hr PRN; dose may be increased up to 1.25 mg Q4–6 hr PRN.**5–11 yr:** Start at 0.31 mg inhaled Q8 hr PRN; dose may be increased to 0.63 mg Q8 hr PRN.**≥12 yr and adult:** Start at 0.63 mg inhaled Q6–8 hr PRN; dose may be increased to 1.25 mg inhaled Q8 hr PRN.***Aerosol inhaler (MDI):*****≥4 yr and adult:** 2 puffs Q4–6 hr PRN

For use in acute exacerbations, more aggressive dosing may be used.



R-isomer of racemic albuterol. Side effects include tachycardia, palpitations, tremor, insomnia, nervousness, nausea, and headache.

Current clinical data in children indicate levalbuterol is as effective as albuterol, with fewer cardiac side effects at equipotent doses (0.31–0.63 mg levalbuterol  $\approx$  2.5 mg albuterol).

More frequent dosing may be necessary in asthma exacerbation.

**LEVETIRACETAM**

Keppra, Keppra XR, and generics

***Anticonvulsant***

No



Yes



2



C

**Tabs:** 250, 500, 750, 1000 mg**Extended-release tabs (Keppra XR):** 500, 750 mg**Oral solution:** 100 mg/mL (480 mL); dye free and contains parabens**Injection:** 100 mg/mL (5 mL); contains 45 mg sodium chloride and 8.2 mg sodium acetate trihydrate per 100 mg drug**Premixed injection:** 500 mg/100 mL in 0.82% sodium chloride, 1000 mg/100 mL in 0.75% sodium chloride, 1500 mg/100 mL in 0.54% sodium chloride***Partial seizures (adjunctive therapy using immediate-release dosage forms):*****Infant (1–5 mo):** Start at 7 mg/kg/dose PO BID; increase by 7 mg/kg/dose BID every 2 wk as tolerated to the recommended dose of 21 mg/kg/dose BID. An average daily dose of 35 mg/kg/24 hr was reported in clinical trials.**Infant ≥ 6 mo–child 3 yr (>20 kg):** Start at 10 mg/kg/dose PO BID; increase by 10 mg/kg/dose BID every 2 wk as tolerated to the recommended dose of 25 mg/kg/dose BID. An average daily dose of 47 mg/kg/24 hr was reported in clinical trials.**Child 4–15 yr:** Start at 10 mg/kg/dose PO BID; increase by 10 mg/kg/dose BID every 2 wk as tolerated up to a **max. dose** of 30 mg/kg/dose BID or 3000 mg/24 hr. An average daily dose of 44 mg/kg/24 hr was reported in clinical trials.***Alternative dosing with oral tablets:*****20–40 kg:** Start at 250 mg PO BID; increase by 250 mg BID every 2 wk as tolerated up to a **maximum** of 750 mg BID.**>40 kg:** Start at 500 mg PO BID; increase by 500 mg BID every 2 wk as tolerated up to a **maximum** of 1500 mg BID.**16 yr–adult:** Start at 500 mg PO BID; may increase by 500 mg/dose BID every 2 wk as tolerated up to a **max. dose** of 1500 mg BID.

LEVETIRACETAM *continued****Mycoclonic seizure (adjunctive therapy using immediate-release dosage forms):***

≥ 12 yr and adult: Start at 500 mg PO BID, then increase dosage by 500 mg/dose BID every 2 wk as tolerated to reach target dosage of 1500 mg BID.

***Tonic-clonic seizure (primary generalized, adjunctive therapy; use immediate-release dosage forms):***

**Child 6–15 yr:** Start at 10 mg/kg/dose PO BID; increase by 10 mg/kg/dose BID every 2 wk as tolerated to reach the target dosage of 30 mg/kg/dose BID.

**16 yr–adult:** Start at 500 mg PO BID; then increase dosage by 500 mg/dose BID every 2 wk as tolerated to reach the target dosage of 1500 mg BID.

***Refractory seizures (add-on therapy [limited data]):*** See remarks.

**Do not** abruptly withdraw therapy to reduce risk for seizures. **Use with caution** in renal impairment (**reduce dose; see Chapter 31**), hemodialysis, and neuropsychiatric conditions.



May cause loss of appetite, vomiting, dizziness, headaches, somnolence, agitation, depression, and mood swings. Drowsiness, fatigue, nervousness, and aggressive behavior have been reported in children. Nonpsychotic behavioral symptoms reported in children is ≈ 3 times greater than in adults (37.6% vs. 13.3%). Suicidal behavior or ideation, serious dermatologic reactions (e.g., Stevens-Johnson syndrome and TEN), and hematologic abnormalities have been reported. Levetiracetam may decrease carbamazepine's effects. Ginkgo may decrease levetiracetam's effects.

Use in children 6 mo–4 yr have been reported in refractory seizures of various types and as an add-on therapy. The following dosage had been used: Start at 5–10 mg/kg/24 hr PO ÷ BID–TID; if needed and tolerated, increase dose by 10 mg/kg/24 hr at weekly intervals up to a **max. dose** of 60 mg/kg/24 hr.

Drug has excellent PO absorption. For IV use, use similar immediate-release PO dosages only when oral route of administration is not feasible. Extended-release tablet is designed for once-daily administration at similar daily dosage of immediate-release forms (e.g., 1000 mg once daily of the extended-release tablet is equivalent to 500 mg BID of the immediate-release tablet).

## LEVOCARNITINE

See Carnitine

## LEVOFLOXACIN

Levaquin, Quixin, Iquix and generics

**Antibiotic, quinolone**



No



Yes



2



C

**Tabs:** 250, 500, 750 mg

**Oral solution:** 25 mg/mL (100, 200, 480 mL)

**Injection:** 25 mg/mL (20, 30 mL)

**Premixed injection in D<sub>5</sub>W:** 250 mg/50 mL, 500 mg/100 mL, 750 mg/150 mL

**Ophthalmic drops:**

**Quixin:** 0.5% (5 mL)

**Iquix:** 1.5% (5 mL)

***Child:***

<5 yr: 10 mg/kg/dose IV/PO Q12 hr; **max. dose** 500 mg/24 hr

≥5 yr: 10 mg/kg/dose IV/PO Q24 hr; **max. dose** 500 mg/24 hr

**Recurrent or persistent acute otitis media (6 mo–<5 yr):** 10 mg/kg/dose PO Q12 hr × 10 days; **max. dose** 500 mg/24 hr

**Community-acquired pneumonia (IDSA/Pediatric Infectious Disease Society):**

**6 mo–<5 yr:** 8–10 mg/kg/dose PO/IV Q12 hr; **max. dose** 750 mg/24 hr

**5–12 yr:** 8–10 mg/kg/dose PO/IV Q24 hr; **max. dose** 750 mg/24 hr



*Continued*

LEVOFLOXACIN *continued***Inhalational anthrax (postexposure) and plague:**

≥6 mo and <50 kg: 8 mg/kg/dose PO/IV Q12 hr; **max. dose** 500 mg/24 hr

>50 kg: 500 mg PO/IV once daily

**Duration of therapy:**

**Inhalational anthrax (postexposure):** 60 days

**Plague:** 10–14 days

**Adult:**

**Community-acquired pneumonia:** 500 mg PO/IV Q24 hr × 7–14 days; *OR* 750 mg PO/IV Q24 hr × 5 days

**Complicated UTI/acute pyelonephritis:** 250 PO/IV Q24 hr × 10 days; *OR* 750 mg PO/IV Q24 hr × 5 days

**Uncomplicated UTI:** 250 mg PO/IV Q24 hr × 3 days

**Uncomplicated skin/skin structure infection:** 500 mg PO/IV Q24 hr × 7–10 days

**Acute bacterial sinusitis:** 500 mg PO/IV Q24 hr × 10–14 days; *OR* 750 mg PO/IV Q24 hr × 5 days

**Inhalational anthrax (post exposure) and plague:** 500 mg PO/IV Q24 hr. **Duration of therapy:** inhalational anthrax, 60 days; plague, 10–14 days.

**Conjunctivitis:**

≥1 yr and adult: Instill 1–2 drops of the 0.5% solution to affected eye(s) Q2 hr up to 8 times/24 hr while awake for the first 2 days, then Q4 hr up to 4 times/24 hr while awake for the next 5 days.

**Corneal ulcer:**

≥6 yr and adult: Instill 1–2 drops of the 1.5% solution to affected eye(s) Q30 min–2 hr while awake and 4 and 6 hr after retiring for the first 3 days, then Q1–4 hr while awake.

**Contraindicated** in hypersensitivity to other quinolones. **Avoid** in patients with history of QTc prolongation or taking QTc-prolonging drugs, and excessive sunlight exposure. **Use with caution** in diabetes, seizures, children <18 yr, and renal impairment (**adjust dose, see Chapter 31**). Ophthalmic solution may cause GI disturbances, headache, and blurred vision. Musculoskeletal disorders (e.g., arthralgia, arthritis, tendinopathy, and gait abnormality) may occur. Peripheral neuropathy has been reported. Safety in pediatric patients treated >14 days has not been evaluated. Like other quinolones, tendon rupture can occur during or after therapy (risk increases with concurrent corticosteroids). Use with NSAIDs may increase risk of CNS stimulation and seizures.

Infuse IV over 1–1.5 hr; **avoid** IV push or rapid infusion because of risk of hypotension. **Do not** administer antacids or other divalent salts with or within 2 hr of oral levofloxacin dose; otherwise may be administered with or without food.

**LEVOTHYROXINE (T<sub>4</sub>)**

Synthroid, Tirosint, Unithroid, Unithroid Direct, and generics

**Thyroid product**

No



No



1




A

**Tabs:** 25, 50, 75, 88, 100, 112, 125, 137, 150, 175, 200, 300 mcg

**Caps (Tirosint):** 13, 25, 50, 75, 88, 100, 112, 125, 137, 150 mcg

**Injection:** 100, 200, 500 mcg; preservative free

**Oral suspension:** 25 mcg/mL 

**Child PO dosing:**

**1–3 mo:** 10–15 mcg/kg/dose once daily. If patient is at risk for developing cardiac failure, start with lower dose of 25 mcg/24 hr. If patient has very low T<sub>4</sub> (<5 mcg/dL) use higher 12–17 mcg/kg/24 hr dose.

**3–6 mo:** 8–10 mcg/kg/dose once daily

**6–12 mo:** 6–8 mcg/kg/dose once daily

**1–5 yr:** 5–6 mcg/kg/dose once daily



LEVOTHYROXINE (T<sub>4</sub>) *continued*

**6–12 yr:** 4–5 mcg/kg/dose once daily

**>12 yr:**

**Incomplete growth and prepuberty:** 2–3 mcg/kg/dose once daily

**Complete growth and puberty:** 1.7 mcg/kg/dose once daily

**Child IM/IV dose:** 50%–75% of oral dose once daily

**Adult:**

**PO:** Start with 12.5–25 mcg/dose once daily. Increase by 25–50 mcg/24 hr at intervals of Q2–4 wk until euthyroid. Usual adult dose: 100–200 mcg/24 hr.

**IM/IV dose:** 50% of oral dose once daily.

**Myxedema coma or stupor:** 200–500 mcg IV  $\times$  1, then 75–300 mcg IV once daily; convert to oral therapy once patient is stabilized.

**Contraindications** include acute MI, thyrotoxicosis, and uncorrected adrenal insufficiency. May cause hyperthyroidism, rash, growth disturbances, hypertension, arrhythmias, diarrhea, and weight loss. Pseudotumor cerebri has been reported in children. Overtreatment may cause craniosynostosis in infants and premature closure of epiphyses in children.



Total replacement dose may be used in children unless there is evidence of cardiac disease; in that case, begin with one fourth of maintenance and increase weekly. Titrate dosage with clinical status and serum T<sub>4</sub> and TSH. Increases effects of warfarin. Phenytoin, rifampin, carbamazepine, iron and calcium supplements, antacids, and orlistat may decrease levothyroxine levels. Tricyclic antidepressants and SSRIs may enhance toxic effects.

**100 mcg levothyroxine = 65 mg thyroid USP.** Administer oral doses on an empty stomach and tablets with a full glass of water. Iron and calcium supplements and antacids may decrease absorption; do not administer within 4 hr of these agents. Excreted in low levels in breast milk; preponderance of evidence suggests no clinically significant effect in infants.

**LIDOCAINE**

Xylocaine, L-M-X, Lidoderm, and various generics

**Antiarrhythmic class Ib, local anesthetic**



Yes



No



1



B

**Injection:** 0.5%, 1%, 1.5%, 2%, 4%, 5%, 10% (1% sol = 10 mg/mL)

**IV infusion (in D<sub>5</sub>W):** 0.4% (4 mg/mL) (250, 500 mL); 0.8% (8 mg/mL) (250 mL)

**Injection with epinephrine (some preparations may contain metabisulfite or are preservative free):**

**Injection with 1:50,000 epi:** 2%

**Injection with 1:100,000 epi:** 1%, 2%

**Injection with 1:200,000 epi:** 0.5%, 1%, 1.5%, 2%

**Ointment:** 5% (30, 50 g)

**Cream, topical:** 3% (30, 85 g), 4% (L-M-X-4 and others) [OTC] (5, 15, 30, 45 g); may contain benzyl alcohol

**Cream, rectal:** 5% (L-M-X-5 and others; 15, 30 g); contains benzyl alcohol

**Gel (external):** 2% (5, 10, 20, 30 mL), 3% (10, 30 mL), 4% (10, 30, 113 g), 5% (10, 30, 113 g); may contain benzyl alcohol, EDTA

**Lotion:** 3% (177 mL)

**Solution (external):** 4% (50 mL); may contain parabens

**Oral solution (mouth/throat):** 2% (4, 15, 100 mL)

**Transdermal patch (Lidoderm):** 5% (30s)

**Topical 2.5% (with 2.5% prilocaine):** See *Lidocaine and Prilocaine*.

*Continued*

LIDOCAINE *continued***Anesthetic:****Injection:**

**Without epinephrine:** **Max. dose** of 4.5 mg/kg/dose (up to 300 mg); do not repeat within 2 hr.

**With epinephrine:** **Max. dose** of 7 mg/kg/dose (up to 500 mg); do not repeat within 2 hr.

**Topical:**

**Cream (child  $\geq$  2 yr and adult):** Apply to affected intact skin areas BID–QID.

**Gel or ointment (child  $\geq$  2 yr and adult):** Apply to affected intact skin areas once daily–QID; **max. dose** 4.5 mg/kg up to 300 mg.

**Patch (adult):** Apply to most painful area with up to 3 patches at a time. Patch(es) may be applied for up to 12 hr in any 24-hr period.

**Antiarrhythmic (infant, child, adolescent):**

**Bolus:** 1 mg/kg/dose (**max. dose** 100 mg) slowly IV; may repeat in 10–15 min  $\times$  2; **max. total dose** 3–5 mg/kg within the first hr. ETT dose = 2–3  $\times$  IV dose.

**Continuous infusion:** 20–50 mcg/kg/min IV/IO (**do not** exceed 20 mcg/kg/min for patients with shock, CHF, hepatic disease, or cardiac arrest); see inside cover for infusion preparation. Administer a 1-mg/kg bolus when infusion is initiated if bolus has not been given within previous 15 min.

**Oral use (viscous liquid):**

**Child ( $\geq$  3 yr):** Up to the lesser of 4.5 mg/kg/dose or 300 mg/dose, swish and spit Q3 hr PRN up to a **max. dose** of 4 doses per 12-hr period.

**Adult:** 15 mL, swish and spit Q3 hr PRN up to a **max. dose** of 8 doses/24 hr.

For cardiac arrest, amiodarone is the preferred agent over lidocaine; lidocaine may be used only when amiodarone is not available.

**Contraindicated** in Stokes-Adams attacks, SA, AV, or intraventricular heart block without a pacemaker.

Side effects include hypotension, asystole, seizures, and respiratory arrest. Anaphylactic reactions have been reported.

CYP 450 2D6 and 3A3/4 substrate. Decrease dose in hepatic failure or decreased cardiac output. **Do not use** topically for teething. Prolonged infusion may result in toxic accumulation of lidocaine, especially in infants. **Do not use** epinephrine-containing solutions for treatment of arrhythmias.

Therapeutic levels 1.5–5 mg/L. Toxicity occurs at  $>7$  mg/L. Toxicity in neonates may occur at  $>5$  mg/L, owing to reduced protein binding of drug. Elimination  $T_{1/2}$ : premature infant, 3.2 hr; adult, 1.5–2 hr.

When using topical patch, avoid exposing application site to external heat sources; may increase risk for toxicity.

**LIDOCAINE AND PRILOCAINE**

EMLA, Oraqix, Eutectic mixture of lidocaine and prilocaine

**Topical anesthetic**

Yes



Yes



?



B

**Cream:** Lidocaine 2.5% + prilocaine 2.5% (5, 30 g)

**Periodontal gel (Oraqix):** Lidocaine 2.5% + prilocaine 2.5% (1.7 g in dental cartridges; 20s)

See Chapter 6 for general use information.

**Neonate ( $\geq$  37-wk gestation):**

**Painful procedures (e.g., IM injections):** 1 g/site for at least 60 min

**Circumcision:** 1–2 g and cover with occlusive dressing for 60–90 min

**Infant and child:** The following are the recommended **max. doses** based on child's age and weight.

LIDOCAINE AND PRILOCAINE *continued*

Age and Weight	Maximum Total EMLA Dose (g)	Maximum Application Area (cm <sup>2</sup> )	Maximum Application Time
Birth—<3 mo or <5 kg	1	10	1 hr
3–12 mo and >5 kg*	2	20	4 hr
1–6 yr and >10 kg	10	100	4 hr
7–12 yr and >20 kg	20	200	4 hr

\*If patient is >3 months and is not >5 kg, use max. total dose that corresponds to patient's weight.  
EMLA, Eutectic mixture of local anesthetics.

**Adult:**

**Minor procedures:** 2.5 g/site for at least 60 min

**Painful procedures:** 2 g/10 cm<sup>2</sup> of skin for at least 2 hr

**Should not be used** in neonates <37 wk of gestation or infants <age 12 mo receiving treatment with methoglobin-inducing agents (e.g., sulfa drugs, acetaminophen, nitrofurantoin, nitroglycerin, nitroprusside, phenobarbital, phenytoin). **Use with caution** in patients with G6PD deficiency, patients treated with class I or III antiarrhythmic drugs (additive or toxic cardiac effects), and in patients with renal and hepatic impairment. Prilocaine has been associated with methemoglobinemia. Long duration of application, large treatment area, small patients, or impaired elimination may result in high blood levels. Apply topically to intact skin and cover with occlusive dressing; **avoid** mucous membranes and eyes. Wipe off cream before procedure.

**LINDANE**

Gamma benzene hexachloride and various generics

**Scabidical agent, pediculocide**



**Shampoo:** 1% (60 mL)

**Lotion:** 1% (60 mL)

**Child and adult (see remarks):**

**Scabies:** Apply thin layer of lotion to skin. Bathe and rinse off medication in adults after 8–12 hr; children 6–8 hr. May repeat × 1 in 7 days PRN.

**Pediculosis capitis:** Apply 15–30 mL of shampoo, lather for 4–5 min, rinse hair and comb with fine comb to remove nits. May repeat × 1 in 7 days PRN.

**Pediculosis pubis:** May use lotion or shampoo (applied locally) as for scabies and pediculosis capitis (see above).



**Contraindicated** in premature infants and seizure disorders. **Use with caution** with drugs that lower seizure threshold. Systemically absorbed. Risk of toxic effects is greater in young children; use other agents (permethrin) in infants, young children (<2 yr), and during pregnancy. Lindane is considered second-line therapy owing to side-effect risk and reports of resistance.



May cause a rash; rarely may cause seizures or aplastic anemia. For scabies, change clothing and bed sheets after starting treatment, and treat family members. For pediculosis pubis, treat sexual contacts.

**Avoid** contact with face, urethral meatus, damaged skin, or mucous membranes. **Do not** use any covering that does not breathe (e.g., plastic lining or clothing) over the applied lindane.

**LINEZOLID**

Zyvox

**Antibiotic, oxazolidinone**

No



No



2



C

**Tabts:** 600 mg; contains  $\approx$  0.45 mEq Na per 200 mg drug**Oral suspension:** 100 mg/5 mL (150 mL); contains phenylalanine and sodium benzoate and 0.8 mEq Na per 200 mg drug**Injection, premixed:** 200 mg in 100 mL, 600 mg in 300 mL; contains 1.7 mEq Na per 200 mg drug**Neonate:**

&lt;1 kg:

&lt;14 days old: 10 mg/kg/dose IV Q12 hr

 $\geq$ 14 days old: 10 mg/kg/dose IV Q8 hr $\geq$ 1 kg:

&lt;7 days old: 10 mg/kg/dose IV/PO Q12 hr

 $\geq$ 7 days old: 10 mg/kg/dose IV/PO Q8 hr $\geq$ 34 wk gestation and 0–28 days old: 10 mg/kg/dose IV/PO Q8 hr**Infant and child < 12 yr old:****Pneumonia, bacteremia, bone/joint infections, septic thrombosis (MRSA), complicated skin/skin structure infections, vancomycin-resistant Enterococcus faecium (VRE) infections (including endocarditis):** 10 mg/kg/dose IV/PO Q8 hr**Uncomplicated skin/skin structure infections:**

&lt;5 yr: 10 mg/kg/dose IV/PO Q8 hr

5–11 yr: 10 mg/kg/dose IV/PO Q12 hr

**Max. dose** for all indications <12 yr: 600 mg/dose $\geq$ 12 yr and adult: 600 mg Q12 hr IV/PO. 400 mg Q12 hr IV/PO may be used for adults with uncomplicated infection. **Duration of therapy:****MRSA infections:** Variable based on response**Pneumonia:** 10–14 days for non-MRSA and 7–21 days (per clinical response) for MRSA**Bacteremia:** 10–28 days**Bone/joint infections:** 3–6 weeks**Skin/skin structure infections:** 10–14 days; longer for complicated cases**Septic thrombosis (MRSA):** 4–6 weeks**VRE infections:** 14–28 days, minimum of 8 weeks for endocarditisMost common side effects include diarrhea, headache, and nausea. Anemia, leukopenia, pancytopenia, thrombocytopenia may occur in patients who are at risk for myelosuppression and receive regimens  $>2$  wk. CBC monitoring recommended in these individuals.

Pseudomembranous colitis and neuropathy (peripheral and optic) have also been reported.

CSF penetration is variable in patients with VP shunts.

Do not use with SSRIs (e.g., fluoxetine, paroxetine), tricyclic antidepressants, venlafaxine, and trazodone; may cause serotonin syndrome. **Avoid** use with MAOIs (e.g., phenelzine) and in patients with uncontrolled hypertension, pheochromocytoma, thyrotoxicosis, and taking sympathomimetics or vasopressor agents (may elevate blood pressure). Patients must **use caution** when consuming large amounts of foods and beverages containing tyramine; may increase blood pressure. Dosing information in severe hepatic failure and renal impairment with multidoses have not been completed.Protect all dosage forms from light and moisture. Oral suspension product must be gently mixed by inverting the bottle 3–5 times before each use (**do not shake**). All oral doses may be administered with or without food.

**LISDEXAMFETAMINE**

Vyvanse

**CNS stimulant**

No



No



X



C

**Capsules:** 20, 30, 40, 50, 60, 70 mg**Attention deficit hyperactivity disorder:****Child ≥ 6 yr and adult:** Start with 30 mg PO QAM. May increase dose by 10–20 mg/24 hr at weekly intervals if needed, up to a **max. dose** of 70 mg/24 hr.

Lisdexamfetamine is a prodrug of dextroamphetamine, which requires activation by intestinal/hepatic metabolism.



**Contraindicated** in amphetamine or sympathomimetic hypersensitivity, symptomatic cardiovascular disease, moderate/severe hypertension, hyperthyroidism, glaucoma, agitated states, drug/alcohol abuse history, and MAOIs (concurrent or use within 14 days). As with other CNS stimulant medications, serious cardiovascular events, including **death**, have been reported in patients with preexisting structural cardiac abnormalities or other serious heart problems. **Use with caution** in patients with hypertension, psychiatric conditions, and epilepsy. May cause insomnia, irritability, rash, appetite suppression/weight loss, dizziness, xerostomia, and GI disturbances. Dermatillomania, Stevens-Johnson syndrome, and TEN have been reported.

Urinary acidifying agents may reduce levels of amphetamines, and urinary alkalizing agents may increase levels. May increase effects of TCAs; increase or decrease effects of guanfacine, phenytoin, and phenobarbital; and decrease effects of adrenergic blockers, antihistamines, and antihypertensives. Norepinephrine may increase effects of amphetamines.

See *Dextroamphetamine ± Amphetamine* for additional remarks.**LISINOPRIL**

Prinivil, Zestril, and generics

**Angiotensin converting enzyme inhibitor, antihypertensive**

No



Yes



3



D

**Tabs:** 2.5, 5, 10, 20, 30, 40 mg**Oral suspension:** 1, 2 mg/mL **Hypertension (see remarks):****Child (<6 yr; limited data):** Use 6–16 yr dosing below.**6–16 yr:** Start with 0.07–0.1 mg/kg/dose PO once daily; **max. initial dose** 5 mg/dose.

If needed, titrate dose upward at 1–2 wk intervals to doses up to 0.61 mg/kg/24 hr or 40 mg/24 hr (higher doses have not been evaluated).

**Adult:** Start with 10 mg PO once daily. If needed, increase dose by 5–10 mg/24 hr at 1–2 wk intervals. Usual dosage range: 10–40 mg/24 hr. **Max. dose:** 80 mg/24 hr.

Use lower initial dose (50% of recommended dose) if using with a diuretic or in the presence of hyponatremia, hypovolemia, and severe CHF.



**Contraindicated** in hypersensitivity and history of angioedema with other ACE inhibitors. Do not use with aliskiren in patients with diabetes. **Avoid** use with dialysis with high-flux membranes; anaphylactoid reactions have been reported. **Use with caution** in aortic or bilateral renal artery stenosis. Side effects include cough, dizziness, headache, hyperkalemia, hypotension (especially with concurrent diuretic or antihypertensive agent use), rash, and GI disturbances. Mood alterations, including depressive symptoms, have been reported.

Continued



LISINOPRIL *continued*

Dual blockade of the renin-angiotensin system with lisinopril and angiotensin receptor antagonist (e.g., losartan) or aliskiren is associated with increased risk for hypotension, syncope, hyperkalemia, and renal impairment. Diabetic patients treated with oral antidiabetic agents should be monitored for hypoglycemia, especially during first month of use. NSAIDs (e.g., indomethacin) may decrease lisinopril's effects. **Adjust dose in renal impairment (see Chapter 31).**

Onset of action: 1 hr, with maximal effect in 6–8 hr. Lisinopril should be discontinued as soon as possible when pregnancy is detected.

**LITHIUM**

Lithobid and many generics (previously available as Eskalith)

**Antimanic agent**

No



Yes



X



D

**Carbonate:**

300 mg carbonate = 8.12 mEq lithium

**Caps:** 150, 300, 600 mg

**Tabs:** 300 mg

**Extended-release tabs:** 300 mg (Lithobid), 450 mg

**Citrate:**

**Syrup:** 8 mEq/5 mL (5, 500 mL); 5 mL is equivalent to 300 mg lithium carbonate

**Child:**

**Initial (immediate-release dosage forms):** 15–60 mg/kg/24 hr ÷ TID–QID PO.

Adjust as needed (weekly) to achieve therapeutic levels.

**Adolescent:** 600–1800 mg/24 hr ÷ TID–QID PO (divided BID using controlled/slow-release tablets).

**Adult:**

**Initial:** 300 mg TID PO. Adjust as needed to achieve therapeutic levels. Usual dose is about 300 mg TID–QID with immediate-release dosage form. For controlled/slow-release tablets, 900–1800 mg/24 hr PO ÷ BID.

**Max. dose:** 2400 mg/24 hr



**Contraindicated** in severe cardiovascular (including Brugada syndrome) or renal disease.

Decreased sodium intake or increased sodium wasting will increase lithium levels.

May cause goiter, nephrogenic diabetes insipidus, hypothyroidism, arrhythmias, or sedation at therapeutic doses.



Coadministration with thiazide diuretics, metronidazole, ACE inhibitors, or NSAIDs may increase risk for lithium toxicity. Iodine may increase risk for hypothyroidism. If used in combination with haloperidol, closely monitor neurologic toxicities, because an encephalopathic syndrome followed by irreversible brain damage has been reported.

**Therapeutic levels:** 0.6–1.5 mEq/L. In either acute or chronic toxicity, confusion and somnolence may be seen at levels of 2–2.5 mEq/L. **Seizures or death** may occur at levels >2.5 mEq/L.

Recommended serum sampling: trough level within 30 min before next scheduled dose.

Steady state is achieved within 4–6 days of continuous dosing. **Adjust dose in renal failure (see Chapter 31).**

**LOPERAMIDE**

Imodium, Imodium A-D, and generics

**Antidiarrheal**

No



No



1



C

**Caps [OTC]:** 2 mg**Tabls [OTC]:** 2 mg**Chewable tabs [OTC]:** 2 mg**Caplets [OTC]:** 2 mg**Oral liquid [OTC]:** 1 mg/5 mL (120 mL); contains 0.5% alcohol**Oral suspension [OTC]:** 1 mg/7.5 mL (120 mL); each 30 mL contains 16 mg of sodium**Acute diarrhea:****Child (initial doses within first 24 hr):****2–5 yr (13–< 21 kg):** 1 mg PO TID**6–8 yr (21–27 kg):** 2 mg PO BID**9–11 yr (>27–43 kg):** 2 mg PO TID**Max. single dose:** 2 mg

Follow initial day's dose with 0.1 mg/kg/dose after each loose stool (not to exceed aforementioned initial doses).

**≥12 yr and adult:** 4 mg/dose × 1, followed by 2 mg/dose after each stool up to **max. dose** of 8 mg/24 hr for adolescents and 16 mg/24 hr for adults.**Chronic diarrhea:****Child:** 0.08–0.24 mg/kg/24 hr ÷ BID–TID; **max. dose** 2 mg/dose

**Contraindicated** in acute dysentery, acute ulcerative colitis, bacterial enterocolitis due to *Salmonella*, *Shigella*, *Campylobacter*, and *Clostridium difficile*, and abdominal pain in the absence of diarrhea. **Avoid** use in children <2 yr owing to reports of paralytic ileus associated with abdominal distention. Rare hypersensitivity reactions, including anaphylactic shock have been reported. May cause nausea, rash, vomiting, constipation, cramps, dry mouth, and CNS depression. **Discontinue use if no clinical improvement is observed within 48 hr.** Naloxone may be administered for CNS depression.

**LORATADINE ± PSEUDOEPHEDRINE**

Alavert, Claritin, Claritin Children's Allergy, Claritin Reditabs, Claritin-D 12 Hour, Claritin-D 24 Hour, many others, and generics

**Antihistamine, less sedating ± decongestant**

Yes



Yes



2



B

**Tabls [OTC]:** 10 mg**Chewable tabs (Claritin Children's Allergy) [OTC]:** 5 mg; contains aspartame**Disintegrating tabs (Reditabs) [OTC]:** 5, 10 mg; contains aspartame**Oral solution or syrup [OTC]:** 1 mg/mL (120 mL); contains propylene glycol and sodium benzoate; some preparations may contain metasulfite**Time-release tabs in combination with pseudoephedrine (PE):**

Claritin-D 12 Hour [OTC]: 5 mg loratadine + 120 mg PE

Claritin-D 24 Hour [OTC]: 10 mg loratadine + 240 mg PE

**Loratadine:****2–5 yr:** 5 mg PO once daily**≥6 yr and adult:** 10 mg PO once daily**Time-release tabs of loratadine and pseudoephedrine:****≥12 yr and adult (see remarks):****Claritin-D 12 Hour:** 1 tablet PO BID**Claritin-D 24 Hour:** 1 tablet PO once daily

Continued

LORATADINE ± PSEUDOEPHEDRINE *continued*

May cause drowsiness, fatigue, dry mouth, headache, bronchospasms, palpitations, dermatitis, and dizziness. Has **not** been implicated in causing cardiac arrhythmias when used with other drugs metabolized by hepatic microsomal enzymes (e.g., ketoconazole, erythromycin). May be administered safely in patients who have allergic rhinitis and asthma.



In hepatic and renal function impairment (GFR < 30 mL/min), prolong loratadine (single agent) dosage interval to every other day. **Adjust dose in renal failure (see Chapter 31).**

For time-release tablets of the combination product (loratadine and pseudoephedrine), prolong dosage interval in renal impairment (GFR < 30 mL/min) as follows: Claritin-D 12 Hour, 1 tablet PO once daily; Claritin-D 24 Hour, 1 tablet PO every other day. **Do not use** the combination product in hepatic impairment; component drugs cannot be individually titrated.

Administer doses on an empty stomach. For use of RediTabs, place tablet on tongue and allow it to disintegrate in the mouth with or without water. For Claritin-D products, also see remarks in *Pseudoephedrine*.

**LORAZEPAM**

Ativan and many generics

**Benzodiazepine anticonvulsant**



Yes



Yes



2



D

**Tabs:** 0.5, 1, 2 mg

**Injection:** 2, 4 mg/mL (each contains 2% benzyl alcohol and propylene glycol)

**Oral solution:** 2 mg/mL (30 mL); alcohol and dye free

**Status epilepticus:**

**Neonate, infant, child, and adolescent:** 0.05–0.1 mg/kg/dose IV over 2–5 min.

May repeat dose in 10–15 min. **Max. dose:** 4 mg/dose.

**Adult:** 4 mg/dose given slowly over 2–5 min. May repeat in 10–15 min. Usual total **max. dose** in 12-hr period is 8 mg.

**Antiemetic adjunct therapy:**

**Child:** 0.02–0.05 mg/kg/dose IV Q6 hr PRN; **max. single dose** is 2 mg.

**Anxiolytic/sedation:**

**Infant and child:** 0.05 mg/kg/dose Q4–8 hr PO/IV; **max. dose** is 2 mg/dose.

May also give IM for preprocedure sedation.

**Adult:** 1–10 mg/24 hr PO ÷ BID–TID

**Contraindicated** in narrow-angle glaucoma and severe hypotension. **Use with caution** in renal insufficiency (glucuronide metabolite clearance is reduced), hepatic insufficiency (may worsen hepatic encephalopathy; decrease dose with severe hepatic impairment), compromised pulmonary function, and use of CNS-depressant medications. May cause respiratory depression, especially in combination with other sedatives. May also cause sedation, dizziness, mild ataxia, mood changes, rash, and GI symptoms. Paradoxical excitation has been reported in children (10%–30% of patients <8 year old).



Significant respiratory depression and/or hypotension has been reported when used in combination with loxapine. Probenecid and valproic acid may increase the effects/toxicity of lorazepam, and oral contraceptive steroids may decrease lorazepam's effects.

Injectable product may be given rectally. Benzyl alcohol and propylene glycol may be toxic to newborns at high doses.

Onset of action for sedation: PO, 20–30 min; IM, 30–60 min; IV, 1–5 min. Duration of action: 6–8 hr.

**Flumazenil is the antidote.**

**LOSARTAN**

Cozaar and generics

**Angiotensin II receptor antagonist**

Yes



Yes



?



C/D

**Tab:** 25, 50, 100 mg**Oral suspension:** 2.5 mg/mL 

Contains 2.12 mg potassium per 25 mg drug

**Hypertension (see remarks):****6–16 yr:** Start with 0.7 mg/kg/dose (**max. dose** of 50 mg/dose) PO once daily.Adjust dose to desired blood pressure response. **Max. dose:** 1.4 mg/kg/24 hr or 100 mg/24 hr.**≥17 yr and adult:** Start with 50 mg PO once daily (use lower initial dose of 25 mg PO once daily if patient receiving diuretics, experiencing intravascular volume depletion, or has hepatic impairment).

Usual maintenance dose is 25–100 mg/24 hr PO ÷ once daily–BID.

**Use with caution** in angioedema (current or past), excessive hypotension (volume depletion), hepatic (use lower starting dose) or renal (contains potassium) impairment, hyperkalemia, renal artery stenosis, and severe CHF. Not recommended in patients <age 6 yr or in children with GFR <30 mL/min/1.73 m<sup>2</sup>, owing to lack of data.

Discontinue use as soon as possible when pregnancy is detected; injury and death to developing fetus may occur. Pregnancy category is "C" during first trimester but changes to "D" for second and third trimesters. Diarrhea, asthenia, dizziness, fatigue, and hypotension are common. Thrombocytopenia, rhabdomyolysis, and angioedema have been rarely reported. Losartan is a substrate for CYP 450 2C9 (major) and 3A4. Fluconazole and cimetidine may increase losartan effects/toxicity. Rifampin, phenobarbital, and indomethacin may decrease its effects. Losartan may increase risk of lithium toxicity. **Do not use** with aliskiren in patients with diabetes or with renal impairment (GFR < 60 mL/min). Dual blockade of the renin-angiotensin system with losartan and ACE inhibitors (e.g., captopril) or aliskiren is associated with increased risk for hypotension, syncope, hyperkalemia, and renal impairment.

**LOW-MOLECULAR-WEIGHT HEPARIN**

See Enoxaparin

**LUCINACTANT**

See Surfactant, pulmonary

**MAGNESIUM CITRATE**

Various generics

16.17% Elemental Magnesium

**Laxative/cathartic**

No



Yes



1



B

**Oral solution [OTC]:** 1.75 g/30 mL (300 mL); 5 mL = 3.9–4.7 mEq Mg**Tab:** 100 mg**Cathartic:****<6 yr:** 2–4 mL/kg/24 hr PO ÷ once daily–BID**6–12 yr:** 100–150 mL/24 hr PO ÷ once daily–BID**>12 yr and adult:** 150–300 mL/24 hr PO ÷ once daily–BID

**Use with caution** in renal insufficiency (monitor magnesium level) and patients receiving digoxin. May cause hypermagnesemia, diarrhea, muscle weakness, hypotension, and respiratory depression. Up to about 30% of dose is absorbed. May decrease absorption of H<sub>2</sub> antagonists, phenytoin, iron salts, tetracycline, steroids, benzodiazepines, and quinolone antibiotics.

**MAGNESIUM HYDROXIDE**

Milk of Magnesia and various generics

41.69% Elemental Magnesium

**Antacid, laxative**

No



Yes



1



B

**Oral liquid [OTC]:** 400 mg/5 mL (Milk of Magnesia and others)**Concentrated oral liquid [OTC]:** 2400 mg/10 mL (Milk of Magnesia concentrate)**Chewable tabs [OTC]:** 400 mg

400 mg magnesium hydroxide is equivalent to 166.76 mg elemental magnesium.

**Combination product with aluminum hydroxide:** See *Aluminum Hydroxide*.**Laxative (all liquid mL doses based on 400 mg/5 mL magnesium hydroxide, unless noted otherwise):**

Dose/24 hr ÷ once daily–QID PO

&lt;2 yr: 0.5 mL/kg

2–5 yr: 5–15 mL **OR** 400–1200 mg (1–3 chewable tabs)6–11 yr: 15–30 mL **OR** 1200–2400 mg (3–6 chewable tabs)≥12 yr and adult: 30–60 mL **OR** 2400–4800 mg (6–12 chewable tabs)**Antacid:****Child:****Liquid:** 2.5–5 mL/dose once daily–QID PO**Tabs:** 400 mg once daily–QID PO**Adult:****Liquid:** 5–15 mL/dose once daily–QID PO**Concentrated liquid (800 mg/5 mL):** 2.5–7.5 mL/dose once daily–QID PO**Tabs:** 400–1200 mg/dose once daily–QID POSee *Magnesium Citrate*. **Use with caution** in renal insufficiency (monitor magnesium level) and patients receiving digoxin. Drink a full 8 oz of liquid with each dose of chewable tablets.**MAGNESIUM OXIDE**

Mag-200, Mag-Ox 400, Uro-Mag, and generics

60.32% Elemental Magnesium

**Oral magnesium salt**

No



Yes



1



B

**Tabs [OTC]:** 200, 250, 400, 420, 500 mg**Caps (Uro-Mag [OTC]):** 140 mg

400 mg magnesium oxide is equivalent to 241.3 mg elemental Mg or 20 mEq Mg.

**Doses expressed in magnesium oxide salt.****Magnesium supplementation:****Child:** 5–10 mg/kg/24 hr ÷ TID–QID PO**Adult:** 400–800 mg/24 hr ÷ BID–QID PO**Hypomagnesemia:****Child:** 65–130 mg/kg/24 hr ÷ QID PO**Adult:** 2000 mg/24 hr ÷ QID POSee *Magnesium Citrate*. **Use with caution** in renal insufficiency (monitor magnesium level) and patients receiving digoxin. For dietary recommended intake (U.S. RDA) for magnesium, see Chapter 21.

**MAGNESIUM SULFATE**

Epsom salts and others  
9.9% Elemental Magnesium  
**Magnesium salt**



No



Yes



1



D

**Injection:** 500 mg/mL (4 mEq/mL) (2, 10, 20, 50 mL)

**Injection, prediluted in sterile water for injection; ready to use:** 40 mg/mL (0.325 mEq/mL) (50, 100, 500, 1000 mL); 80 mg/mL (0.65 mEq/mL) (50 mL)

**Injection, prediluted in D<sub>5</sub>W; ready to use:** 10 mg/mL (0.081 mEq/mL) (100 mL); 20 mg/mL (0.163 mEq/mL) (500 mL)

**Granules:** Approx. 40 mEq Mg per 5 g (454, 1810 g)

500 mg magnesium sulfate is equivalent to 49.3 mg elemental Mg or 4.1 mEq Mg.

**All doses expressed in magnesium sulfate salt.**

**Cathartic:**

**Child:** 0.25 g/kg/dose PO Q4–6 hr

**Adult:** 10–30 g/dose PO Q4–6 hr

**Hypomagnesemia or hypocalcemia:**

**IV/IM:** 25–50 mg/kg/dose Q4–6 hr × 3–4 doses; repeat PRN; **max. single dose:** 2 g

**PO:** 100–200 mg/kg/dose QID PO

**Daily maintenance:**

30–60 mg/kg/24 hr or 0.25–0.5 mEq/kg/24 hr IV

**Max. dose:** 1 g/24 hr

**Adjuvant therapy for moderate to severe reactive airway disease exacerbation (bronchodilation):**

**Child:** 25–75 mg/kg/dose (**max. dose:** 2 g) × 1 IV over 20 min

**Adult:** 2 g/dose × 1 IV over 20 min



When given IV **beware** of hypotension, respiratory depression, complete heart block, and/or hypermagnesemia. Calcium gluconate (IV) should be available as **antidote**. **Use with caution** in patients with renal insufficiency (monitor magnesium levels) and patients on digoxin. **Serum level–dependent toxicity** includes the following: >3 mg/dL: CNS depression; >5 mg/dL: decreased deep tendon reflexes, flushing, somnolence; and >12 mg/dL: respiratory paralysis, heart block.

**Max. IV intermittent infusion rate:** 1 mEq/kg/hr or 125 mg MgSO<sub>4</sub> salt/kg/hr

Pregnancy category is "D" because hypocalcemia, osteopenia, and fractures in the developing baby or fetus have been reported in pregnant women receiving magnesium >5–7 days for preterm labor.

**MANNITOL**

Aridol, Osmitol, Resectisol, and various generics  
**Osmotic diuretic**



No



Yes



?



C

**Injection:** 50, 100, 150, 200, 250 mg/mL (5%, 10%, 15%, 20%, 25%, respectively)

**Irrigation solution (Resectisol):** 50 mg/mL (5%)

**Anuria/oliguria (child and adult):**

**Test dose to assess renal function:** 0.2 g/kg/dose (**max. dose:** 12.5 g) IV over 3–5 min. If there is no diuresis within 2 hr, discontinue mannitol.

**Initial:** 0.5–1 g/kg/dose IV over 2–6 hr

**Maintenance:** 0.25–0.5 g/kg/dose Q4–6 hr IV over 2–6 hr



**Contraindicated** in severe renal disease, active intracranial bleed, dehydration, and pulmonary edema. May cause circulatory overload and electrolyte disturbances. For hyperosmolar therapy, keep serum osmolality at 310–320 mOsm/kg.



*Continued*

MANNITOL *continued*

**Caution:** Drug may crystallize at low temperatures with concentrations  $\geq 15\%$ ; redissolve crystals by warming solution up to  $70^{\circ}\text{C}$  with agitation. Use an in-line filter. May cause hypovolemia, headache, and polydipsia. Reduction in ICP occurs in 15 min and lasts 3–6 hr.

**MEBENDAZOLE**

Vermox and others

**Anthelmintic**

Yes



No



1



C

**Chewable tabs:** 100 mg (may be swallowed whole or chewed) (boxes of 12s)

**Child (>2 yr) and adult:**

**Pinworms (*Enterobius*):** 100 mg PO  $\times$  1, repeat in 2 wk if not cured.

**Hookworms, roundworms (*Ascaris*), and whipworm (*Trichuris*):** 100 mg PO BID  $\times$  3 days.

Repeat in 3–4 wk if not cured. Alternatively, may administer 500 mg PO  $\times$  1.

**Capillariasis:** 200 mg PO BID  $\times$  20 days

**Visceral larva migrans (*toxocariasis*):** 100–200 mg PO BID  $\times$  5 days

**Trichinellosis (*Trichinella spiralis*):** 200–400 mg PO TID  $\times$  3 days, then 400–500 mg PO TID  $\times$  10 days; use with steroids for severe symptoms.

**Ancylostoma caninum (eosinophilic enterocolitis):** 100 mg PO BID  $\times$  3 days.

See latest edition of the AAP *Red Book* for additional information.

Experience in children <2 yr and in pregnancy is limited. May cause rash, headache, diarrhea, and abdominal cramping in cases of massive infection. Liver function test elevations and hepatitis have been reported with prolonged courses; monitor hepatic function with prolonged therapy. Family may need to be treated as a group. Therapeutic effect may be decreased if administered to patients receiving aminoquinolones, carbamazepine, or phenytoin. Cimetidine may increase effects/toxicity of mebendazole. Administer with food. Tablets may be crushed and mixed with food, swallowed whole, or chewed.

**MEDROXYPROGESTERONE**

Depo-Provera, Provera, and various generics; Depo-Sub Q

Provera 104

**Contraceptive, progestin**

Yes



No



2



X

**Tabs (Provera and generics):** 2.5, 5, 10 mg

**Injection, suspension as acetate:**

Depo-Provera and generics, for IM use only: 150 mg/mL (1 mL), 400 mg/mL (2.5 mL); may contain parabens

**Injection, prefilled syringe as acetate:**

Depo-Sub Q Provera 104, for SC use only: 104 mg (0.65 mL of 160 mg/mL); contains parabens

**Adolescent and adult:**

**Contraception:** Initiate therapy during first 5 days after onset of a normal menstrual period, within 5 days postpartum if not breast feeding, or if breast feeding, at 6-wk postpartum. When converting contraceptive method to Depo-Sub Q Provera, dose should be administered within 7 days after last day of using previous method (pill, ring, patch).

**IM (Depo-Provera):** 150 mg Q3 mo

**SC (Depo-Sub Q Provera 104):** 104 mg Q3 mo (Q12–14 wk)

MEDROXYPROGESTERONE *continued***Adolescent and adult:****Amenorrhea:** 5–10 mg PO once daily  $\times$  5–10 days**Abnormal uterine bleeding:** 5–10 mg PO once daily  $\times$  5–10 days, initiated on 16th or 21st day of menstrual cycle**Endometriosis-associated pain (Depo-Sub Q Provera 104):** 104 mg SC Q3 mo. **Do not use**  $>2$  yr, owing to impact on bone mineral density.

Consider patient's risk for osteoporosis because of potential for decrease in bone mineral density with long-term use. **Contraindicated** in pregnancy, breast or genital cancer, liver disease, missed abortion, thrombophlebitis, thromboembolic disorders, cerebral vascular disease, and undiagnosed vaginal bleeding. **Use with caution** in patients with family history of breast cancer, depression, diabetes, and fluid retention. May cause dizziness, headache, insomnia, fatigue, nausea, weight increase, appetite changes, amenorrhea, and breakthrough bleeding. Cholestatic jaundice and increased ICP have been reported.

Aminoglutethimide may decrease medroxyprogesterone levels. May alter thyroid and liver function tests, prothrombin time, factors VII, VIII, IX and X, and metyrapone test.

Do not inject IM or SC product intravenously. Shake IM injection vial well before use, and administer in upper arm or buttock. Administer SC injection product into anterior thigh or abdomen. Administer oral doses with food.

**MEFLOQUINE HCL**

Lariam and generics

**Antimalarial**

Yes



No



2



C

**Tabs:** 250 mg (228 mg base)**Doses expressed in mg mefloquine HCl salt****Malaria prophylaxis (start 1 wk before exposure and continue for 4 wk after leaving endemic area):****Child (PO, administered Q weekly):** **$<10$  kg:** 5 mg/kg**10–19 kg:** 62.5 mg ( $\frac{1}{4}$  tablet)**20–30 kg:** 125 mg ( $\frac{1}{2}$  tablet)**31–45 kg:** 187.5 mg ( $\frac{3}{4}$  tablet) **$>45$  kg:** 250 mg (1 tablet)**Adult:** 250 mg PO Q weekly**Malaria treatment (uncomplicated/mild infection, chloroquine-resistant Plasmodium vivax):****Child  $\geq 6$  mo and  $> 5$  kg:** 15 mg/kg  $\times$  1 PO, followed by 10 mg/kg  $\times$  1 PO 12 hr later (**max. total dose:** 1250 mg)**Adult:** 750 mg  $\times$  1 PO, followed by 500 mg  $\times$  1 PO 12 hr laterSee latest edition of AAP *Red Book* for additional information.

**Contraindicated** in active or recent history of depression, anxiety disorders, psychosis or schizophrenia, seizures, or hypersensitivity to quinine or quinidine. **Use with caution** in cardiac dysrhythmias and neurologic disease. May cause dizziness, headache, syncope, psychiatric symptoms (e.g., anxiety, paranoia, depression, hallucinations, psychotic behavior), seizures, ocular abnormalities, GI symptoms, leukopenia, and thrombocytopenia. Most adverse events occur within 3 doses with prophylaxis use. Monitor liver enzymes and ocular examinations for therapies  $>1$  yr.

Mefloquine is a substrate and inhibitor of P-glycoprotein and may reduce valproic acid levels. ECG abnormalities may occur when used in combination with quinine, quinidine, chloroquine,

*Continued*



MEFLOQUINE HCL *continued*

halofantrine, and  $\beta$ -blockers. If any of the aforementioned antimalarial drugs is used in the initial treatment of severe malaria, initiate mefloquine at least 12 hours after the last dose of any of these drugs. **Do not** initiate halofantrine or ketoconazole within 15 days of last dose of mefloquine. Use with chloroquine may increase risk for seizures. Rifampin may decrease mefloquine levels.

**Do not** take on an empty stomach. Administer with at least 240 mL (8 oz) water. Treatment failures in children may be related to vomiting of administered dose. If vomiting occurs <30 min after dose, administer a second full dose. If vomiting occurs 30–60 min after dose, administer an additional half-dose. If vomiting continues, monitor patient closely and consider alternative therapy.

**MEROPENEM**

Merrem and generics

**Carbapenem antibiotic**

No



Yes



2



B

**Injection:** 0.5, 1 g

Contains 3.92 mEq Na/g drug

**Neonate (IV):**

**Non-CNS intraabdominal infections with meropenem MIC <4 mcg/mL based on population PK modeling:**

**<32 wk' gestation:**

**<14 days old:** 20 mg/kg/dose IV Q12 hr

**≥14 days old:** 20 mg/kg/dose IV Q8 hr

**≥32 wk' gestation:**

**<14 days old:** 20 mg/kg/dose IV Q8 hr

**≥14 days old:** 30 mg/kg/dose IV Q8 hr

**Non-CNS intraabdominal infections with meropenem MIC 4–8 mcg/mL (moderately resistant) from a single-dose PK simulation study:**

**>30 wk' gestation and >7 days old:** 40 mg/kg/dose IV Q8 hr

**Infant ≥ 1–3 mo (IV):**

**Non-CNS intraabdominal infections with meropenem MIC <4 mcg/mL based on population PK modeling:** 20–30 mg/kg/dose Q8 hr

**Meningitis (recommended dose from 2004 IDSA meningitis practice guidelines):** 40 mg/kg/dose Q8 hr

**Infant ≥ 3 mo, child, and adolescent (IV):**

**Skin and subcutaneous tissue infections:** 30 mg/kg/24 hr ÷ Q8 hr; **max. dose:** 1.5 g/24 hr

**Intraabdominal and mild/moderate infections, and fever/neutropenia empirical therapy:** 60 mg/kg/24 hr ÷ Q8 hr; **max. dose:** 3 g/24 hr

**Meningitis, severe infections, cystic fibrosis pulmonary exacerbations:** 120 mg/kg/24 hr ÷ Q8 hr.

**Max. dose:** 6 g/24 hr

**Adult (IV):**

**Skin and subcutaneous tissue infections:** 1.5 g/24 hr ÷ Q8 hr

**Intraabdominal and mild/moderate infections, and fever/neutropenia empirical therapy:** 1 g Q8 hr

**Meningitis and severe infections:** 2 g ÷ Q8 hr

**Contraindicated** in patients sensitive to carbapenems or with a history of anaphylaxis to  $\beta$ -lactam antibiotics. **Use with caution** in meningitis and CNS disorders (may cause seizures) and renal impairment (**adjust dose [see Chapter 31]**). Drug penetrates well into CSF.

May cause diarrhea, rash, nausea, vomiting, oral moniliasis, glossitis, pain and irritation at IV injection site, and headache. Hepatic enzyme and bilirubin elevation, dermatologic reactions (including Stevens-Johnson syndrome and TEN), leukopenia, thrombocytopenia (in renal dysfunction) and neutropenia have been reported. Probenecid may increase serum meropenem levels. May reduce valproic acid levels.



**MESALAMINE**

Apriso, Asacol, Asacol HD, Canasa, Delzicol, Lialda, Pentasa, Rowasa, SfRowasa, and others; 5-aminosalicylic acid, 5-ASA

**Salicylate, GI antiinflammatory agent**



Yes



Yes



2



B/C

**Caps, controlled release:**

**Pentasa:** 250, 500 mg

**Delzicol:** 400 mg

**Apriso:** 375 mg; contains aspartame

**Tab, delayed-release:** 400 mg (Asacol), 800 mg (Asacol HD), 1200 mg (Lialda)

**Suppository (Canasa):** 1000 mg (30s, 42s)

**Rectal suspension (Rowasa, SfRowasa, and others):** 4 g/60 mL; contains sulfites (SfRowasa is sulfite free) and sodium benzoate

**Child:**

**Caps, controlled release:** 50 mg/kg/24 hr ÷ Q6–12 hr PO; **max. dose:** 1 g/dose

**Tab, delayed release:** 50 mg/kg/24 hr ÷ Q8–12 hr PO; **max. dose:** 4.8 g/24 hr

**Adult (ulcerative colitis):****Caps, controlled release:**

**Initial therapy:** 1 g QID PO × 3–8 wk

**Maintenance therapy for remission:**

**Apriso:** 1.5 g QAM PO

**Pentasa:** 1 g QID PO

**Tab, delayed-release:**

**Initial therapy:**

**Asacol:** 800 mg TID PO × 6 wk

**Asacol HD:** 1.6 g TID PO × 6 wk

**Lialda:** 2.4–4.8 g once daily PO up to 8 wk

**Maintenance therapy for remission:**

**Asacol:** 1.6 g/24 hr PO in divided doses

**Lialda:** 2.4 g PO once daily

**Suppository:** 1000 mg QHS PR × 3–6 wk, retaining each dose in rectum for 1–3 hr or longer if possible.

**Rectal suspension:** 60 mL (4 g) QHS × 3–6 wk, retaining each dose for ≈ 8 hr; lying on left side during administration improves delivery to sigmoid colon.



Generally **not recommended** in children <16 yr with chicken pox or flulike symptoms (risk of Reye syndrome). **Contraindicated** in active peptic ulcer disease, severe renal failure, and salicylate hypersensitivity. Rectal suspension should not be used in patients with history of sulfite allergy. **Use with caution** in sulfasalazine hypersensitivity, impaired hepatic or renal function, pyloric stenosis, and concurrent thrombolytics. May cause headache, GI discomfort, pancreatitis, pericarditis, rash, and Stevens-Johnson syndrome.

**Do not** administer with lactulose or other medications that can lower intestinal pH. Oral capsules are designed to release medication throughout the GI tract, and oral tablets release medication at the terminal ileum and beyond. Mesalamine 400 mg PO is equivalent to 1 g sulfasalazine PO. Tablets should be swallowed whole.

May cause a false-positive urinary normetanephrine test. All products are pregnancy category "B" except for Asacol HD, which is pregnancy category "C."

**METFORMIN**

Glucophage, Glucophage XR, Glumetza, Fortamet, Riomet, and generics

**Antidiabetic, biguanide**

Yes



Yes



2



B

**Tabs:** 500, 850, 1000 mg**Tabs, extended release:****Glucophage XR and others:** 500, 750 mg**Fortamet, Glumetza, and others:** 500, 1000 mg**Oral suspension (Riomet):** 100 mg/mL (120, 480 mL); contains saccharin**Administer all doses with meals (e.g., BID with morning and evening meals).****Child (10–16 yr) (see remarks):** Start with 500 mg BID; may increase dose weekly by500 mg/24 hr in 2 divided doses up to a **max. dose** of 2000 mg/24 hr.**Child ≥ 17 yr and adult (see remarks):****500 mg tabs:** Start with 500 mg PO BID; may increase dose weekly by 500 mg/24 hr in 2 divided doses up to a **max. dose** of 2500 mg/24 hr. Administer 2500 mg/24 hr doses by dividing daily dose TID with meals.**850 mg tabs:** Start with 850 mg PO once daily with morning meal; may increase by 850 mg every 2 wk up to a **max. dose** of 2550 mg/24 hr (first dosage increment: 850 mg PO BID; second dosage increment: 850 mg PO TID).**Extended-release tabs:** Start with 500 mg PO once daily with evening meal; may increase by 500 mg every wk up to a **max. dose** of 2000 mg/24 hr (if glycemic control is not achieved at max. dose, divide dose to 1000 mg PO BID). If a dose > 2000 mg is needed, switch to non-extended-release tablets in divided doses, and increase dose to a **max. dose** of 2550 mg/24 hr.**Contraindicated** in renal impairment, hepatic impairment (increased risk for lactic acidosis), CHF, metabolic acidosis, and during radiology studies using iodinated contrast media. **Use with caution** when transferring patients from chlorpropamide therapy (potential hypoglycemia risk) or for patients with excessive alcohol intake, hypoxemia, dehydration, surgical procedures, hepatic disease, anemia, and thyroid disease.**Fatal lactic acidosis** (diarrhea, severe muscle pain, cramping, shallow and fast breathing, unusual weakness and sleepiness) and decrease in vitamin B<sub>12</sub> levels have been reported. May cause GI discomfort (~50% incidence), anorexia, and vomiting. Transient abdominal discomfort or diarrhea have been reported in 40% of pediatric patients. Cimetidine, furosemide, and nifedipine may increase effects/toxicity of metformin. In addition to monitoring serum glucose and glycosylated hemoglobin, monitor renal function and hematologic parameters (baseline and annual).

Adult patients initiated on 500 mg PO BID may also have their dose increased to 850 mg PO BID after 2 wk.

**COMBINATION THERAPY WITH SULFONYLUREAS:** If patient has not responded to 4 wk of maximum doses of metformin monotherapy, consider gradual addition of an oral sulfonylurea, with continued maximum metformin dosing (even if failure with sulfonylurea has occurred). Attempt to identify minimum effective dosage for each drug (metformin and sulfonylurea), because the combination can increase risk for sulfonylurea-induced hypoglycemia. If patient does not respond to 1–3 mo of combination therapy with maximum metformin doses, consider discontinuing combination therapy and initiating insulin therapy.

Administer all doses with food.

**METHADONE HCL**

Dolophine, Methadose, and generics

**Narcotic, analgesic**

No



Yes



2



C

**Tabs:** 5, 10 mg**Tabs (dispersible):** 40 mg**Oral solution:** 5 mg/5 mL, 10 mg/5 mL; contains 8% alcohol**Concentrated solution:** 10 mg/mL**Injection:** 10 mg/mL (20 mL), contains 0.5% chlorobutanol**Analgesia:****Child:** 0.7 mg/kg/24 hr PO, SQ, IM, or IV ÷ Q4–6 hr PRN for pain; **max. dose:** 10 mg/dose**Adult:** 2.5–10 mg/dose Q3–4 hr PO, SQ, IM, or IV PRN for pain**Detoxification or maintenance:** See package insert.

Unintentional overdoses have resulted in fatalities and severe adverse events, such as respiratory depression and cardiac arrhythmias. May cause respiratory depression, sedation, increased ICP, hypotension, and bradycardia. Average  $T_{1/2}$ : children 19 hr, adults 35 hr. Oral duration of action is 6–8 hr initially and 22–48 hr after repeated doses. Respiratory effects last longer than analgesia. Accumulation may occur with continuous use, making it necessary to adjust dose. Nevirapine may decrease serum levels of methadone. Methadone is a substrate for CYP 450 3A3/4, 2D6, and 1A2 and an inhibitor of 2D6.

See Chapter 6 for equianalgesic dosing and onset of action. **Adjust dose in renal failure** (see Chapter 31).

**METHIMAZOLE**

Tapazole and generics

**Antithyroid agent**

No



No



2



D

**Tabs:** 5, 10 mg**Hyperthyroidism:****Child:****Initial:** 0.4–0.7 mg/kg/24 hr or 15–20 mg/m<sup>2</sup>/24 hr PO ÷ Q8 hr**Maintenance:** 1/3–2/3 of initial dose PO ÷ Q8 hr**Max. dose:** 30 mg/24 hr**Adult:****Initial:** 15–60 mg/24 hr PO ÷ TID**Maintenance:** 5–15 mg/24 hr PO ÷ TID

Readily crosses placental membranes and distributes into breast milk (maternal doses ≤20 mg/24 hr considered safe, but data are insufficient to support safe use with maternal doses >20 mg/24 hr). Blood dyscrasias, dermatitis, hepatitis, arthralgia, CNS reactions, pruritus, nephritis, hypoprothrombinemia, agranulocytosis, headache, fever, and hypothyroidism may occur.

May increase effects of oral anticoagulants. When correcting hyperthyroidism, existing  $\beta$ -blocker, digoxin, and theophylline doses may have to be reduced to avoid potential toxicities.

Switch to maintenance dose when patient is euthyroid. Administer all doses with food.



**METHYLDOPA**

Various brand names

**Central  $\alpha$ -adrenergic blocker, antihypertensive**

Yes



Yes



1



B/C

**Tabs:** 250, 500 mg**Injection:** 50 mg/mL (5 mL); may contain sulfites**Oral suspension:** 50 mg/mL **Hypertension:****Child:** 10 mg/kg/24 hr  $\div$  Q6–12 hr PO; increase PRN Q2 days. **Max. dose:**

65 mg/kg/24 hr or 3 g/24 hr, whichever is less.

**Adult:** 250 mg/dose BID–TID PO. Increase PRN Q2 days to **max. dose** of 3 g/24 hr.**Hypertensive crisis:****Child:** 2–4 mg/kg/dose IV. If no response within 4–6 hr, may increase dose to 5–10 mg/kg/dose IV; give doses Q6–8 hr. **Max. dose** (whichever is less): 65 mg/kg/24 hr or 3 g/24 hr.**Adult:** 250–1000 mg IV Q6–8 hr; **max. dose:** 4 g/24 hr**Contraindicated** in pheochromocytoma and active liver disease. **Use with caution** if patient is receiving haloperidol, propranolol, lithium, or sympathomimetics. Positive Coombs test rarely associated with hemolytic anemia. Fever, leukopenia, sedation, memory impairment, hepatitis, GI disturbances, orthostatic hypotension, black tongue, and gynecomastia may occur. May interfere with laboratory tests for creatinine, urinary catecholamines, uric acid, and AST.May increase AV blocking effects of  $\beta$ -blockers and antihypertensive effects of other antihypertensives.  $\alpha_2$ -Antagonist antidepressants, serotonin/norepinephrine reuptake inhibitors, and methylphenidate may reduce antihypertensive effects of methyldopa. **Do not use** in combination with MAOIs (may enhance adverse effects of methyldopa). **Do not coadminister** oral doses with iron; decreases methyldopa absorption. **Adjust dose in renal failure** (see Chapter 31).

Pregnancy category is "C" for injectable dosage form and "B" for oral dosage forms.

**METHYLENE BLUE**

Many generics

**Antidote, drug-induced methemoglobinemia and cyanide toxicity**

No



Yes



3



X

**Injection:** 10 mg/mL (1%) (1, 10 mL)**Methemoglobinemia:****Child and adult:** 1–2 mg/kg/dose or 25–50 mg/m<sup>2</sup>/dose IV over 5 min. May repeat in 1 hr if needed.At high doses, may cause methemoglobinemia. **Avoid** subcutaneous or intrathecal routes of administration. **Use with caution** in G6PD deficiency or renal insufficiency. May cause nausea, vomiting, dizziness, headache, diaphoresis, stained skin, and abdominal pain.

Causes blue-green discoloration of urine and feces.

Serotonin syndrome has been reported with coadministration of SSRIs, SNRIs, or clomipramine. Use with bupropion, paroxetine, sertraline, duloxetine, vilazodone, venlafaxine, fluoxetine, or desipramine is considered contraindicated.

**METHYLPHENIDATE HCL**

Ritalin, Methylin, Metadate ER, Methylin ER, Concerta, Ritalin SR, Metadate CD, Ritalin LA, Daytrana, Quillivant XR, and generics

**CNS stimulant**



No



No



3



C

**Tabs:** 5, 10, 20 mg

**Chewable tabs:** 2.5, 5, 10 mg; contains phenylalanine

**Oral solution (Methylin and generics):** 1 mg/mL, 2 mg/mL; may contain propylene glycol

**Oral suspension (Quillivant XR):** 25 mg/5 mL (60, 120, 150, 180 mL); contains sodium benzoate

**Extended-release tabs:**

**8-hr duration (Metadate ER):** 20 mg

**24-hr duration (Concerta):** 18, 27, 36, 54 mg

**Sustained-release tabs:**

**8-hr duration (Ritalin SR):** 20 mg

**Extended-release caps:**

**24-hr duration (Metadate CD, Ritalin LA):** 10, 20, 30, 40, 50, 60 mg

**Transdermal patch (Daytrana):** 10 mg/9 hr (each 12.5 cm<sup>2</sup> patch contains 27.5 mg), 15 mg/9 hr (each 18.75 cm<sup>2</sup> patch contains 41.3 mg), 20 mg/9 hr (each 25 cm<sup>2</sup> patch contains 55 mg), 30 mg/9 hr (each 37.5 cm<sup>2</sup> patch contains 82.5 mg) (30s)

**Attention deficit hyperactivity disorder:**

**Immediate-release oral dosage forms (Methylin, Ritalin [ $\geq 6$  yr]):**

**Initial:** 0.3 mg/kg/dose (or 2.5–5 mg/dose) given before breakfast and lunch.

May increase by 0.1 mg/kg/dose PO (or 5–10 mg/24 hr) weekly until maintenance dose achieved. May give extra afternoon dose if needed.

**Maintenance dose range:** 0.3–1 mg/kg/24 hr

**Max. dose:** 2 mg/kg/24 hr or 60 mg/24 hr

**Extended-release once-daily oral dosage form (Concerta [ $\geq 6$  yr]):**

**Methylphenidate-naïve patients:** Start with 18 mg PO QAM for children and adolescents and 18–36 mg PO QAM for adults. Dosage may be increased at weekly intervals in 18-mg increments up to the following **max. doses:**

**6–12 yr:** 54 mg/24 hr

**13–17 yr:** 72 mg/24 hr, **not to exceed** 2 mg/kg/24 hr

**Patients currently receiving methylphenidate:** See following table.

**Recommended Dose Conversion from Methylphenidate Regimens to Concerta**

Previous Methylphenidate Daily Dose	Recommended Concerta Dose
5 mg PO BID–TID or 20 mg SR PO once daily	18 mg PO QAM
10 mg PO BID–TID or 40 mg SR PO once daily	36 mg PO QAM
15 mg PO BID–TID or 60 mg SR PO once daily	54 mg PO QAM
20 mg PO BID–TID	72 mg PO QAM

After a week of receiving above recommended Concerta dose, dose may be increased in 18-mg increments at weekly intervals up to a **max.** of 54 mg/24 hr for 6–12 yr and 72 mg/24 hr (**not to exceed** 2 mg/kg/24 hr) for 13–17 yr.

**Other extended-release oral dosage forms:**

**Metadate CD ( $\geq 6$  yr):** Start with 20 mg PO once daily; dosage may be increased at weekly intervals in 20-mg increments up to a **max. dose** of 60 mg/24 hr.

**Ritalin LA ( $\geq 6$  yr):** Start with 20 mg PO once daily; dosage may be increased at weekly intervals in 10-mg increments up to a **max. dose** of 60 mg/24 hr.

**Transdermal patch (Daytrana):** Apply to the hip 2 hr before effect is needed, and remove 9 hr later. Patch may be removed before 9 hr if shorter duration of effect is desired or if late-day adverse effects appear.

*Continued*

METHYLPHENIDATE HCL *continued***Transdermal patch (Daytrana):**

**6–17 yr:** Start with 10 mg/9-hr patch once daily. Increase dose PRN Q7 days by increasing to next dosage strength.

**Contraindicated** in glaucoma, anxiety disorders, motor tics, and Tourette syndrome. Medication should generally **not** be used in children <age 5 yr; diagnosis of ADHD in this age group is extremely difficult and should only be done in consultation with a specialist. Sudden death (children, adolescents, and adults), stroke (adults), and MI (adults) have been reported in patients with preexisting structural cardiac abnormalities or other serious heart problems.



**Use with caution** in patients with hypertension, psychiatric conditions, and epilepsy. Insomnia, weight loss, anorexia, rash, nausea, emesis, abdominal pain, hypertension or hypotension, tachycardia, arrhythmias, palpitations, restlessness, headaches, fever, tremor, visual disturbances, and thrombocytopenia may occur. Abnormal liver function, cerebral arteritis and/or occlusion, peripheral vasculopathy (including Raynaud phenomenon), leukopenia and/or anemia, hypersensitivity reactions, transient depressed mood, paranoia, mania, auditory hallucination, priapism, and scalp hair loss have been reported. Skin irritation may occur, and contact dermatitis has been reported with transdermal route. High doses may slow growth by appetite suppression. GI obstruction has been reported with Concerta.

May increase serum concentrations/effects of tricyclic antidepressants, dopamine agonists (e.g., haloperidol), phenytoin, phenobarbital, and warfarin. May decrease effects of antihypertensive drugs. Effect of methylphenidate may be potentiated by MAOIs; hypertensive crisis may also occur if used within 14 days of discontinuance of MAOI.

**Extended/sustained-release dosage forms have either an 8- or 24-hour dosage interval (as stipulated previously).** Concerta dosage form delivers 22.2% of its dose as an immediate-release product, with the remaining amounts as an extended-release product (e.g., 18-mg strength: 4 mg as immediate release and 14 mg as extended release). **Do not** consume alcohol with Ritalin LA or Metadate CD dosage forms; may result in more rapid release of drug. **Do not** expose transdermal application site to external heat sources (e.g., electric blankets, heating pads); may increase drug release.

**METHYLPREDNISOLONE**

Medrol, Medrol Dosepack, Solu-Medrol, Depo-Medrol, and generics

**Corticosteroid**

No



No



2



C

**Tabs:** 2, 4, 8, 16, 24, 32 mg

**Tabs, dose pack (Medrol Dosepack and others):** 4 mg (21s)

**Injection, Na succinate (Solu-Medrol and others):** 40, 125, 500, 1000, 2000 mg (IV or IM use); may contain benzyl alcohol

**Injection, Acetate (Depo-Medrol and others):** 20, 40, 80 mg/mL (IM repository); may contain polyethylene glycol (1, 5 mL)

**Anti-inflammatory/immunosuppressive:**

**PO/IM/IV:** 0.5–1.7 mg/kg/24 hr ÷ Q6–12 hr



**Asthma exacerbations (2007 National Heart, Lung, and Blood Institute Guideline Recommendations; dose until peak expiratory flow reaches 70% of predicted or personal best):**

**Child ≤ 12 yr (IM/IV/PO):** 1–2 mg/kg/24 hr ÷ Q12 hr (**max. dose:** 60 mg/24 hr). Higher alternative regimen of 1 mg/kg/dose Q6 hr × 48 hr, followed by 1–2 mg/kg/24 hr (**max. dose:** 60 mg/24 hr) ÷ Q12 hr has been suggested.

**>12 yr and adult (IV/IM/PO):** 40–80 mg/24 hr ÷ Q12–24 hr

METHYLPREDNISOLONE *continued***Outpatient asthma exacerbation burst therapy (longer durations may be necessary):****PO:****Child ≤ 12 yr:** 1–2 mg/kg/24 hr ÷ Q12–24 hr (**max. dose:** 60 mg/24 hr) × 3–10 days.**Child > 12 yr and adult:** 40–60 mg/24 hr ÷ Q12–24 hr × 3–10 days.**IM (use methylprednisolone acetate product) for patients vomiting or with adherence issues:****Child ≤ 12 yr:** 7.5 mg/kg (**max. dose:** 240 mg) IM × 1**Child > 12 yr and adult:** 240 mg IM × 1**Acute spinal cord injury:**

30 mg/kg IV over 15 min, followed in 45 min by a continuous infusion of 5.4 mg/kg/hr × 23 hr

**See Chapter 30** for relative steroid potencies and doses based on BSA. Acetate form may also be used for intraarticular and intralesional injection and has longer times to max. effect and duration of action; it should **NOT** be given IV. Like all steroids, may cause hypertension, pseudotumor cerebri, acne, Cushing syndrome, adrenal axis suppression, GI bleeding, hyperglycemia, and osteoporosis.

Barbiturates, phenytoin, and rifampin may enhance methylprednisolone clearance. Erythromycin, itraconazole, and ketoconazole may increase methylprednisolone levels. Methylprednisolone may increase cyclosporine and tacrolimus levels.

**METOCLOPRAMIDE**

Reglan, Maxolon, Metozolv, and many generics

**Antiemetic, prokinetic agent**

No



Yes



2



B

**Tabs:** 5, 10 mg**Tabs, orally disintegrating (ODT [Metozolv]):** 5 mg**Injection:** 5 mg/mL (2 mL)**Oral solution:** 5 mg/5 mL**Gastroesophageal reflux (GER) or GI dysmotility:****Infant and child:** 0.1–0.2 mg/kg/dose up to QID IV/IM/PO; **max. dose:** 0.8 mg/kg/24 hr**Adult:** 10–15 mg/dose QAC and QHS IV/IM/PO**Antiemetic (all ages):** Premedicate with diphenhydramine to reduce EPS.

1–2 mg/kg/dose Q2–6 hr IV/IM/PO

**Postoperative nausea and vomiting:****Child:** 0.1–0.2 mg/kg/dose Q6–8 hr PRN IV**>14 yr and adult:** 10 mg Q6–8 hr PRN IV

**Contraindicated** in GI obstruction, seizure disorder, pheochromocytoma, or in patients receiving drugs likely to cause extrapyramidal symptoms (EPS). May cause EPS, especially at higher doses. Sedation, headache, anxiety, depression, leukopenia, and diarrhea may occur.

Neuroleptic malignant syndrome and tardive dyskinesia (increased risk with prolonged duration of therapy; avoid use >12 weeks) have been reported.

For GER, give 30 min before meals and at bedtime. **Reduce dose in renal impairment (see Chapter 31).**



**METOLAZONE**

Zaroxolyn and many generics

*Diuretic, thiazide-like*

Yes



Yes



2



B

**Tabs:** 2.5, 5, 10 mg**Oral suspension:** 0.25, 1 mg/mL **Dosage based on Zaroxolyn (for oral suspension, see remarks):****Child:** 0.2–0.4 mg/kg/24 hr ÷ once daily–BID PO**Adult:****Hypertension:** 2.5–5 mg once daily PO**Edema:** 2.5–20 mg once daily PO

**Contraindicated** in patients with anuria, hepatic coma, or hypersensitivity to sulfonamides or thiazides. Use with caution in severe renal disease, impaired hepatic function, gout, lupus erythematosus, diabetes mellitus, and elevated cholesterol and triglycerides. Electrolyte imbalance, GI disturbance, hyperglycemia, marrow suppression, chills, hyperuricemia, chest pain, hepatitis, and rash may occur.

Oral suspensions have increased bioavailability; lower doses may be necessary when using these dosage forms. More effective than thiazide diuretics in impaired renal function; may be effective in GFRs as low as 20 mL/min. Furosemide-resistant edema in pediatric patients may benefit from addition of metolazone.

Pregnancy category changes to "D" if used for pregnancy-induced hypertension.

**METOPROLOL**

Lopressor, Toprol-XL, and generics

*Adrenergic blocking agent ( $\beta_1$ -selective), class II antiarrhythmic*

Yes



No



1



C

**Tabs:** 25, 50, 100 mg**Extended-release tabs (Toprol-XL and generics):** 25, 50, 100, 200 mg**Oral liquid:** 10 mg/mL **Injection:** 1 mg/mL (5 mL)**Hypertension:****Child ≥ 1 yr and adolescent:**

**Non-extended-release oral dosage forms:** Start at 1–2 mg/kg/24 hr PO ÷ BID; **max. dose:** 6 mg/kg/24 hr up to 200 mg/24 hr.

**Extended-release tabs (≥6 yr and adolescent):** Start at 1 mg/kg/dose (**max. dose:** 50 mg) PO once daily; if needed, adjust dose up to a **max. dose** of 2 mg/kg/24 hr or 200 mg/24 hr once daily (higher doses have not been evaluated).

**Adult:**

**Non-extended-release tabs:** Start at 50–100 mg/24 hr PO ÷ once daily–BID; if needed, increase dosage at weekly intervals to desired blood pressure. Usual effective dosage range is 100–450 mg/24 hr. Doses >450 mg/24 hr have not been studied. Patients with bronchospastic diseases should receive the lowest possible daily dose ÷ TID.

**Extended-release tabs:** Start at 25–100 mg/24 hr PO once daily; if needed, increase dosage at weekly intervals to desired blood pressure. Usual dosage range is 50–100 mg/24 hr. Doses >400 mg/24 hr have not been studied.

METOPROLOL *continued*

**Contraindicated** in sinus bradycardia, heart block >1st degree, sick sinus syndrome (except with functioning pacemaker), cardiogenic shock, and uncompensated CHF. **Use with caution** in hepatic dysfunction, peripheral vascular disease, history of severe anaphylactic hypersensitivity drug reactions, pheochromocytoma, and concurrent use with verapamil, diltiazem, or anesthetic agents that may decrease myocardial function. Should not be used with bronchospastic diseases. Reserpine and other drugs that deplete catecholamines (e.g., MAOIs) may increase effects of metoprolol. Metoprolol is a CYP 450 2D6 substrate.

**Avoid** abrupt cessation of therapy in ischemic heart disease; angina, ventricular arrhythmias, and MI have occurred. Common side effects include bradyarrhythmia, heart block, heart failure, pruritus, rash, GI disturbances, dizziness, fatigue, and depression. Bronchospasm, dyspnea, and elevations in transaminase, alkaline phosphatase, and LDH have all been reported.

**METRONIDAZOLE**

Flagyl, Flagyl ER, Protostat, MetroGel, MetroLotion, MetroCream, Noritate, MetroGel-Vaginal, and generics

**Antibiotic, antiprotozoal**



Yes



Yes



3





B

**Tab:** 250, 500 mg

**Tab, extended release (Flagyl ER):** 750 mg

**Caps:** 375 mg

**Oral suspension:** 10 mg/mL or 50 mg/mL 

**Oral syrup:** 5 mg/mL 

**Injection:** 500 mg; contains 830 mg mannitol/g drug

**Ready-to-use injection:** 5 mg/mL (100 mL); contains 28 mEq Na/g drug

**Gel, topical (MetroGel):** 0.75% (28, 60 g)

**Lotion (MetroLotion):** 0.75% (60 mL); contains benzyl alcohol

**Cream, topical:**

**MetroCream:** 0.75% (45 g); contains benzyl alcohol

**Noritate:** 1% (30 g)

**Gel, vaginal (MetroGel-Vaginal):** 0.75% (70 g with 5 applicators)

**Amebiasis:**

**Child:** 35–50 mg/kg/24 hr PO ÷ TID × 10 days

**Adult:** 500–750 mg/dose PO TID × 10 days

**Anaerobic infection:**

**Neonate, PO/IV:**

**<7 days:**

**<1.2 kg:** 7.5 mg/kg/dose Q48 hr

**1.2–2 kg:** 7.5 mg/kg/dose Q24 hr

**≥2 kg:** 15 mg/kg/24 hr ÷ Q12 hr

**≥7 days:**

**<1.2 kg:** 7.5 mg/kg Q24 hr

**1.2–2 kg:** 15 mg/kg/24 hr ÷ Q12 hr

**≥2 kg:** 30 mg/kg/24 hr ÷ Q12 hr

**Infant/child/adult:**

**IV/PO:** 30 mg/kg/24 hr ÷ Q6 hr; **max. dose:** 4 g/24 hr

*Continued*

METRONIDAZOLE *continued***Other parasitic infections:****Infant/child:** 15–30 mg/kg/24 hr PO ÷ Q8 hr**Adult:** 250 mg PO Q8 hr or 2 g PO × 1**Bacterial vaginosis:****Adolescent and adult:****PO:****Immediate-release tabs:** 500 mg BID × 7 days**Extended-release tabs:** 750 mg once daily × 7 days**Vaginal:** 5 g (1 applicator full) BID × 5 days**Giardiasis:****Child:** 15 mg/kg/24 hr PO ÷ TID × 5 days; **max. dose:** 750 mg/24 hr**Adult:** 250 mg PO TID × 5 days**Trichomoniasis:** Treat sexual contacts.**Child:** 15 mg/kg/24 hr PO ÷ TID × 7 days; **max. dose:** 2000 mg/24 hr**Adolescent/adult:** 2 g PO × 1; **OR** 250 mg PO TID **OR** 375 mg PO BID × 7 days**Clostridium difficile infection (IV may be less efficacious):****Child:** 30 mg/kg/24 hr ÷ Q6 hr PO/IV × 10 days; **max. dose:** 2000 mg/24 hr**Adult:** 250–500 mg TID–QID PO × 10–14 days, or 500 mg Q8 hr IV × 10–14 days**Helicobacter pylori infection (use in combination with amoxicillin and bismuth subsalicylate):****Child:** 15–20 mg/kg/24 hr ÷ BID PO × 4 wk**Adult:** 250–500 mg TID PO × 14 days**Inflammatory bowel disease (as alternative to sulfasalazine):****Adult:** 400 mg BID PO**Topical use:** Apply and rub a thin film into affected areas at the following frequencies specific to product concentration:**0.75% cream:** BID**1% cream:** Once daily

**Avoid** use in first-trimester pregnancy. **Use with caution** in patients with CNS disease, blood dyscrasias, severe liver or **renal disease (GFR < 10 mL/min)**; see **Chapter 31**. If using single 2-g dose in a breast-feeding mother, discontinue breast-feeding for 12 to 24 hours to allow excretion of drug.

Nausea, diarrhea, urticaria, dry mouth, leukopenia, vertigo, metallic taste, and peripheral neuropathy may occur. Candidiasis may worsen. May discolor urine. Patients **should not** ingest alcohol for 24–48 hr after dose (disulfiram-type reaction).

Single-dose oral regimen no longer recommended in bacterial vaginosis (poor efficacy). May increase levels or toxicity of phenytoin, lithium, and warfarin. Phenobarbital and rifampin may increase metronidazole metabolism.

IV infusion must be given slowly over 1 hr. For IV use in all ages, some references recommend a 15 mg/kg loading dose.



**MICAFUNGIN SODIUM**

Mycamine

*Antifungal, echinocandin*

Yes



Yes



?



C

**Injection:** 50, 100 mg; contains lactose**Invasive candidiasis (see remarks):****Neonate and infant (based on a multidose pharmacokinetic and safety trial in 13 neonates/infants >48 hr and <120 days old with suspected or invasive candidiasis; minimum of 4–5 days of therapy):****<1 kg:** 10 mg/kg/dose IV once daily; additional data from another multidose trial in 12 preterm neonates (median birth weight: 775 g, 27 wk' gestation) suggest 15 mg/kg/dose IV once daily will provide similar AUC drug exposure of  $\approx$  5 mg/kg/dose in adults. **$\geq$ 1 kg:** 7 mg/kg/dose IV once daily**Child and adolescent:** 3–4 mg/kg/dose IV once daily; **max. dose:** 200 mg/dose**Adult:** 100–150 mg IV once daily**Esophageal candidiasis (see remarks):****Child and adult:****<50 kg:** 3–4 mg/kg/dose IV once daily; **max. dose:** 200 mg/dose **$\geq$ 50 kg:** 150 mg IV once daily; mean duration for successful therapy was 15 days (range, 10–30 days).**Candida prophylaxis in hematopoietic stem cell transplant:****Child and adult:****<50 kg:** 1.5 mg/kg/dose IV once daily; **max. dose:** 50 mg/dose **$\geq$ 50 kg:** 50 mg IV once daily**Invasive aspergillosis (see remarks; doses under investigation):****Child and adult:****<50 kg:** 3–4 mg/kg/dose IV once daily; dosages as high as 7.5 mg/kg/24 hr have been tolerated. **$\geq$ 50 kg:** 150 mg IV once daily

Prior hypersensitivity to other echinocandins (anidulafungin, caspofungin) increases risk; anaphylaxis with shock has been reported. **Use with caution** in hepatic and renal impairment.

No dosing adjustments are required based on race or gender, or in patients with severe renal dysfunction or mild to moderate hepatic function impairment. Effect of severe hepatic function impairment on micafungin pharmacokinetics has not been evaluated. Higher dosage requirements in premature and young infants may be due to faster drug clearance secondary to lower protein binding. Higher treatment doses in infants and children have been reported at 8.6–12 mg/kg/dose IV once daily.

May cause GI disturbances, phlebitis, rash, hyperbilirubinemia, liver function test elevation, headache, fever, and rigor. Anemia, leukopenia, neutropenia, thrombocytopenia, and hemolysis have been reported. Micafungin is a CYP 450 3A isoenzyme substrate and weak inhibitor. May increase effects/toxicity of nifedipine and sirolimus.

**MICONAZOLE**

Topical products: Micatin, Lotrimin AF, and others

Vaginal products: Monistat, Vagistat-3, and others

**Antifungal agent**

No



No



2



C

**Cream [OTC]:** 2% (15, 30, 90 g)**Lotion [OTC]:** 2% (30, 60 mL)**Ointment [OTC]:** 2% (28.4 g)**Solution [OTC]:** 2% with alcohol (30.3 mL)**Gel [OTC]:** 2% with alcohol (24 g)**Topical solution [OTC]:** 2% with alcohol (30.3 mL)**Powder [OTC]:** 2% (70, 90 g)**Spray, liquid [OTC]:** 2% (105 mL); contains alcohol**Spray, powder [OTC]:** 2% (85, 90, 100 g); contains alcohol**Vaginal cream [OTC]:** 2% (15, 25, 45 g), 4% (15, 25 g)**Vaginal suppository [OTC]:** 100 mg (7s), 200 mg (3s)**Vaginal combination packs:****Monistat 1 Combination Pack [OTC]:** 1200 mg suppository (1) and 2% cream (9 g)**Monistat 3, Vagistat-3 [OTC]:** 200 mg suppository (3s) and 2% cream (9 g)**Monistat 7 [OTC]:** 100 mg suppository (7s) and 2% cream (9 g)**Topical:** Apply BID  $\times$  2–4 wk.**Vaginal:****7-day regimen:** 1 applicator full of 2% cream or 100 mg suppository QHS  $\times$  7 days**3-day regimen:** 1 applicator full of 4% cream or 200 mg suppository QHS  $\times$  3 days**Monistat 1:** 1200 mg suppository  $\times$  1 at bedtime or during the day**Use with caution** in hypersensitivity to other imidazole antifungal agents (e.g., clotrimazole, ketoconazole). Side effects include pruritus, rash, burning, phlebitis, headaches, and pelvic cramps.

Drug is a substrate and inhibitor of the CYP 450 3A3/4 isoenzymes. Vaginal use with concomitant warfarin use has also been reported to increase warfarin's effect. Vegetable oil base in vaginal suppositories may interact with latex products (e.g., condoms and diaphragms); consider switching to vaginal cream.

**Avoid** contact with eyes.**MIDAZOLAM**

Various generics; previously available as Versed

**Benzodiazepine**

Yes



Yes



2



D

**Injection:** 1, 5 mg/mL; some preparations may contain 1% benzyl alcohol**Oral syrup:** 2 mg/mL; contains sodium benzoate**Titrate to effect under controlled conditions.** See Chapter 6 for additional routes of administration.**Sedation for procedures:****Child:****IV:**

**6 mo–5 yr:** 0.05–0.1 mg/kg/dose over 2–3 min. May repeat dose PRN in 2–3-min intervals up to a **max. total dose** of 6 mg. A total dose up to 0.6 mg/kg may be necessary for desired effect.

**6–12 yr:** 0.025–0.05 mg/kg/dose over 2–3 min. May repeat dose PRN in 2–3 min intervals up to a **max. total dose** of 10 mg. A total dose up to 0.4 mg/kg may be necessary for desired effect.

**>12–16 yr:** Use adult dose, up to **max. total dose** of 10 mg.

MIDAZOLAM *continued***PO:**

≥ **6 mo:** 0.25–0.5 mg/kg/dose × 1. **Max. dose:** 20 mg. Younger patients (6 mo–5 yr) may require higher doses of 1 mg/kg/dose, whereas older patients (6–15 yr) may require only 0.25 mg/kg/dose. Use 0.25 mg/kg/dose for patients with cardiac or respiratory compromise, concurrent CNS-depressive drug, or high-risk surgery.

**Adult:**

**IV:** 0.5–2 mg/dose over 2 min. May repeat PRN in 2–3-min intervals until desired effect. Usual total dose: 2.5–5 mg; **max. total dose:** 10 mg.

**Sedation with mechanical ventilation:****Intermittent:**

**Infant and child:** 0.05–0.15 mg/kg/dose IV Q1–2 hr PRN

**Continuous IV infusion (initial doses, titrate to effect):****Neonate:**

<32 wk' gestation: 0.5 mcg/kg/min

≥32 wk' gestation: 1 mcg/kg/min

**Infant and child:** 1–2 mcg/kg/min

**Refractory status epilepticus:**

≥ **2 mo and child:** Load with 0.15 mg/kg IV × 1, followed by a continuous infusion of 1 mcg/kg/min; titrate dose upward Q5 min to effect (mean dose of 2.3 mcg/kg/min [range, 1–18 mcg/kg/min] has been reported).

**Contraindicated** in patients with narrow angle glaucoma and shock. **Use with caution** in CHF, renal impairment (adjust dose [see Chapter 31]), pulmonary disease, hepatic dysfunction, and in neonates. Causes respiratory depression, hypotension, and bradycardia.

Cardiovascular monitoring is recommended. Use lower doses or reduce dose when given in combination with narcotics or in patients with respiratory compromise.

Higher recommended dosage for younger patients (6 mo–5 yr) is attributed to water-soluble properties of midazolam and higher percentage of body water for younger patients.

Drug is a substrate for CYP 450 3A4. Serum concentrations may be increased by cimetidine, clarithromycin, diltiazem, erythromycin, itraconazole, ketoconazole, and protease inhibitors (use contraindicated). Sedative effects may be antagonized by theophylline. **Effects can be reversed by flumazenil.** For pharmacodynamic information, see Chapter 6.

**MILRINONE**

Primacor and generics

**Inotrope**

No



Yes



?



C

**Injection:** 1 mg/mL (10, 20, 50 mL)

**Premixed injection in D<sub>5</sub>W:** 200 mcg/mL (100, 200 mL)

**Child (limited data):** 50 mcg/kg IV bolus over 15 min, followed by a continuous infusion of 0.25–0.75 mcg/kg/min and titrate to effect.



**Adult:** 50 mcg/kg IV bolus over 10 min, followed by a continuous infusion of 0.375–0.75 mcg/kg/min and titrate to effect. **Max. dose:** 1.13 mg/kg/24 hr.

**Contraindicated** in severe aortic stenosis, severe pulmonic stenosis, and acute MI. May cause headache, dysrhythmias, hypotension, hypokalemia, nausea, vomiting, anorexia, abdominal pain, hepatotoxicity, and thrombocytopenia. Pediatric patients may require higher mcg/kg/min doses because of a faster elimination  $T_{1/2}$  and larger volume of distribution than adults. Hemodynamic effects can last up to 3–5 hr after discontinuation of infusion in children.



**Reduce dose in renal impairment.**

**MINERAL OIL**

Kondremul, Fleet Mineral Oil, and generics

**Laxative, lubricant**

No



No



3



C

**Liquid, oral [OTC]:** 480 mL**Emulsion, oral (Kondremul [OTC]):** 480 mL; each 5 mL Kondremul contains 2.5 mL mineral oil**Rectal liquid (Fleet Mineral Oil [OTC]):** 133 mL**Constipation:****Child 5–11 yr (see remarks):****Oral liquid:** 5–15 mL/24 hr ÷ once daily–TID PO**Oral emulsion (Kondremul):** 10–30 mL/24 hr ÷ once daily–TID PO**Rectal:** 66.5 mL as single dose**Child ≥ 12 yr and adult (see remarks):****Oral liquid:** 15–45 mL/24 hr ÷ once daily–TID PO**Oral emulsion (Kondremul):** 30–90 mL/24 hr ÷ once daily–TID PO**Rectal:** 133 mL as single dose

May cause diarrhea, cramps, and lipid pneumonitis via aspiration. Use as a laxative **should not exceed** >1 wk. Onset of action is ≈ 6–8 hr. Higher doses may be necessary to achieve desired effect. **Use with caution** and **do not** give QHS dose in children <5 yr to minimize risk of aspiration. May impair absorption of fat-soluble vitamins, calcium, phosphorus, oral contraceptives, and warfarin. Emulsified preparations are more palatable and dosed differently than oral liquid preparation.



For disimpaction, doses up to 1 ounce (30 mL) per yr of age (**max. dose** of 240 mL) BID can be given.

**MINOCYCLINE**

Minocin, Dynacin, Arestin, Solodyn, and generics

**Antibiotic, tetracycline derivative**

Yes



Yes



X



D

**Tabs:** 50, 75, 100 mg**Caps:** 50, 75, 100 mg**Extended-release tabs (Solodyn):** 45, 65, 90, 115, 135 mg**Caps (pellet filled):** 50, 100 mg**Sustained-release microspheres (Arestin):** 1 mg (12s)**Oral suspension:** 50 mg/5 mL (60 mL); contains 5% alcohol**General infections:**

**Child (8–12 yr):** 4 mg/kg/dose × 1 PO, then 2 mg/kg/dose Q12 hr PO; **max. dose:** 200 mg/24 hr

**Adolescent and adult:** 200 mg/dose × 1 PO, then 100 mg Q12 hr PO

**Chlamydia trachomatis/Ureaplasma urealyticum:**

**Adolescent and adult:** 100 mg PO Q12 hr × 7 days

**Acne (≥12 yr–adult):**

**Immediate-release dosage forms:** 50–100 mg PO once daily–BID

**Extended-release tabs:**

**45–54 kg:** 45 mg PO once daily

**55–77 kg:** 65 mg PO once daily

**78–102 kg:** 90 mg PO once daily

**103–125 kg:** 115 mg PO once daily

**126–136 kg:** 135 mg PO once daily



MINOCYCLINE *continued*

**Not recommended** for children <8 yr and during last half of pregnancy (risk of permanent tooth discoloration). **Use with caution** in renal failure; lower dosage may be necessary. High incidence of vestibular dysfunction (30%–90%). Nausea, vomiting, allergy, increased ICP, photophobia and injury to developing teeth may occur. Hepatitis, including autoimmune hepatitis, liver failure, hypersensitivity reactions (e.g., anaphylaxis, Stevens-Johnson syndrome, erythema multiforme), and lupus-like syndrome have been reported.

May increase effects/toxicity of warfarin and decrease efficacy of live attenuated oral typhoid vaccine. May be administered with food but **NOT** with milk or dairy products. See *Tetracycline* for additional drug/food interactions and comments.

**MINOXIDIL**

Various generics (previously available as Loniten), Rogaine, Men's Rogaine Extra Strength

**Antihypertensive agent, hair growth stimulant**



No



Yes



2



C

**Tabs:** 2.5, 10 mg

**Topical solution:**

**Rogaine and generics [OTC]:** 2% (60 mL)

**Men's Rogaine Extra Strength and generics [OTC]:** 5% (60, 120 mL); contains 30% alcohol

**Topical aerosol foam:**

**Men's Rogaine Extra Strength [OTC]:** 5% (60 g); contains alcohol

**Child < 12 yr:**

Start with 0.1–0.2 mg/kg/24 hr PO once daily. **Max. dose:** 5 mg/24 hr. Dose may be increased in increments of 0.1–0.2 mg/kg/24 hr at 3-day intervals. Usual effective range: 0.25–1 mg/kg/24 hr PO ÷ once daily–BID. **Max. dose:** 50 mg/24 hr.

**≥ 12 yr and adult:**

**Oral:** Start with 5 mg once daily. Dose may be gradually increased at 3-day intervals. Usual effective range: 10–40 mg/24 hr ÷ once daily–BID. **Max. dose:** 100 mg/24 hr.

**Topical (alopecia; see remarks):**

**Adult:** Apply topically to the affected areas of the scalp BID (QAM and QHS).



**Contraindicated** in acute MI, dissecting aortic aneurysm, and pheochromocytoma. Concurrent use with a  $\beta$ -blocker and diuretic is recommended to prevent reflex tachycardia and reduce water retention, respectively. May cause drowsiness, dizziness, CHF, pulmonary edema, pericardial effusion, pericarditis, thrombocytopenia, leukopenia, Stevens-Johnson syndrome, and hypertrichosis (reversible) with systemic use.



Concurrent use of guanethidine may cause profound orthostatic hypotension; use with other antihypertensive agents may cause additive hypotension. Patients with renal failure or receiving dialysis may require a dosage reduction. Antihypertensive onset of action within 30 min and peak effects within 2–8 hr.

**TOPICAL USE:** Local irritation, contact dermatitis may occur. **Do not use** in conjunction with other topical agents (i.e., topical corticosteroids, retinoids, or petrolatum) or agents known to enhance cutaneous drug absorption. Onset of hair growth is 4 mo. Wash hands thoroughly after each application. The 5% solution is flammable.



**MOMETASONE FUROATE ± FORMOTEROL FUMARATE**

Asmanex Twisthaler, Nasonex, Elocon and other generic topical products

In combination with formoterol: Dulera

**Corticosteroid**



No



No



2



C

**Nasal spray (Nasonex):** 0.05%, 50 mcg per actuation (17 g = 120 doses)

**Powder for inhalation, breath activated (Asmanex Twisthaler [see remarks]):** 110 mcg per actuation (7, 14, 30 units), 220 mcg per actuation (14, 60, 120 units); contains lactose

**Topical cream and ointment (Elocon and generics):** 0.1% (15, 45 g)

**Topical lotion and solution (Elocon and others):** 0.1% (30, 60 mL); contains isopropyl alcohol

**In combination with formoterol:**

**Aerosol inhaler (Dulera):**

100 mcg mometasone furoate + 5 mcg formoterol fumarate dihydrate per inhalation (8.8 g delivers 60 inhalations, 13 g delivers 120 inhalations)

200 mcg mometasone furoate + 5 mcg formoterol fumarate dihydrate per inhalation (8.8 g delivers 60 inhalations, 13 g delivers 120 inhalations)

**MOMETASONE FUROATE:**

**Intranasal (allergic rhinitis):** Patients with known seasonal allergic rhinitis should initiate therapy 2–4 wk before anticipated pollen season.

**2–11 yr:** 50 mcg (1 spray) each nostril once daily

**≥12 yr and adult:** 100 mcg (2 sprays) each nostril once daily

**Oral inhalation:**

**4–11 yr:** Start with 110 mcg (1 inhalation) QHS of the 110 mcg inhaler regardless of prior therapy.

**Max. dose:** 110 mcg/24 hr

**≥12 yr and adult:** Max. effects may not be achieved until 1–2 wk or longer. Titrate doses to lowest effective dose once asthma stabilized.

**Previously treated with bronchodilators alone or with inhaled corticosteroids:** Start with 220 mcg (1 inhalation) QHS. Dose may be increased up to a **max. dose** of 440 mcg/24 hr ÷ QHS or BID.

**Previously treated with oral corticosteroids:** Start with 440 mcg BID; **max. dose:** 880 mcg/24 hr.

**Topical (see Chapter 30 for topical steroid comparisons):**

**Cream and ointment:**

**≥2 yr and adult:** Apply a thin film to affected area once daily. Safety and efficacy for >3 wk has not been established for pediatric patients.

**Lotion:**

**≥12 yr and adult:** Apply a few drops to affected area, massaging lightly into skin until it disappears, once daily.

**MOMETASONE FUROATE + FORMOTEROL FUMARATE (Dulera):**

**≥12 yr and adult:** Two inhalations BID of either 100 mcg mometasone + 5 mcg formoterol or 200 mcg mometasone + 5 mcg formoterol based on prior asthma therapy (see table below). **Max. dose:** Two inhalations BID of 200 mcg mometasone + 5 mcg formoterol.

Previous Therapy	Recommended Starting Dose	Recommended Maximum Daily Dose
Medium-dose inhaled corticosteroids	100 mcg mometasone + 5 mcg formoterol: 2 inhalations BID	400 mcg mometasone + 20 mcg formoterol
High-dose inhaled corticosteroids	200 mcg mometasone + 5 mcg formoterol: 2 inhalations BID	800 mcg mometasone + 20 mcg formoterol

Concurrent administration with ketoconazole and other CYP 450 3A4 inhibitors (e.g., protease inhibitors) may increase mometasone levels, resulting in Cushing syndrome and adrenal suppression.

MOMETASONE FUROATE ± FORMOTEROL FUMARATE *continued*

**INTRANASAL:** Clear nasal passages and shake nasal spray well before each use. Onset of action for nasal symptoms of allergic rhinitis has been shown to occur within 11 hr after first dose. Nasal burning and irritation may occur. Nasal septal perforation and taste/smell disturbances have been rarely reported.

**ORAL INHALATION (all forms):** Rinse mouth after each use. Fever, allergic rhinitis, URI, UTI, GI discomfort, and sore throat have been reported in children. Musculoskeletal pain, oral candidiasis, arthralgia, and fatigue may occur. May potentially worsen fungal, bacterial, viral, or parasitic infection, tuberculosis, or ocular herpes simplex. Do not use Asmanex Twisthaler if allergic to milk proteins.

**MOMETASONE + FORMOTEROL (Dulera):** Breast-feeding information is currently unknown. Common side effects include nasopharyngitis, sinusitis, and headache. Angioedema and anaphylaxis have been reported. See *Formoterol* for additional remarks.

**TOPICAL USE:** HPA axis suppression and skin atrophy have been reported with cream and ointment use in infants 6–23 mo. Avoid application/contact to face, eyes, underarms, groin, and open skin. Occlusive dressings and use in diaper dermatitis are not recommended.

**MONTELUKAST**

Singulair and generics

**Antiasthmatic, antiallergy leukotriene receptor antagonist**



No



No



?



B

**Chewable tabs:** 4, 5 mg; contains phenylalanine

**Tabs:** 10 mg

**Oral granules:** 4 mg per packet (30s)

**Asthma and seasonal allergic rhinitis:**

**Child (6 mo–5 yr):** 4 mg (oral granules or chewable tablet) PO QHS; minimum age for use in asthma (per product label) is 12 mo.

**Child (6–14 yr):** 5 mg (chewable tablet) PO QHS

**≥15 yr and adult:** 10 mg PO QHS

**Prevention of exercise-induced bronchospasm (administer dose at least 2 hr before exercise; additional doses should not be administered within 24 hr):**

**Child (6–14 yr):** 5 mg (chewable tablet) PO

**≥15 yr and adult:** 10 mg PO

Chewable tablet dosage form is **contraindicated** in phenylketonuric patients. Side effects include headache, abdominal pain, dyspepsia, fatigue, dizziness, cough, and elevated liver enzymes. Diarrhea, epistaxis, eosinophilia, thrombocytopenia, hypersensitivity reactions (including Stevens-Johnson syndrome and TEN), pharyngitis, nausea, otitis, sinusitis, and viral infections have been reported in children. Neuropsychiatric events, including aggression, anxiety, dream abnormalities, hallucinations, depression, suicidal behavior, and insomnia have been reported.

Drug is a substrate for CYP 450 3A4 and 2C9. Phenobarbital and rifampin may induce hepatic metabolism to increase clearance of montelukast.

Doses may administered with or without food.



**MORPHINE SULFATE**

Roxanol, MS Contin, Oramorph SR, Avinza, Kadian, and many others

**Narcotic, analgesic**

No



Yes



2



C/D

**Oral solution:** 10 mg/5 mL, 20 mg/5 mL**Concentrated oral solution:** 100 mg/5 mL**Caps/tabs:** 15, 30 mg**Controlled-release tabs (MS Contin, Oramorph SR):** 15, 30, 60, 100, 200 mg**Extended-release tabs:** 15, 30, 60, 100, 200 mg**Soluble tabs:** 10, 15, 30 mg**Extended-release caps:****Avinza (10% of dose as immediate release):** 30, 45, 60, 75, 90, 120 mg**Kadian:** 10, 20, 30, 40, 50, 70, 80, 100, 130, 150, 200 mg**Generics:** 10, 20, 30, 50, 60, 80, 100 mg**Rectal suppository:** 5, 10, 20, 30 mg**Injection:** 0.5, 1, 2, 4, 5, 8, 10, 15, 25, 50 mg/mL

Titrate to effect.

**Analgesia/tetralogy (cyanotic) spells:****Neonate:** 0.05–0.2 mg/kg/dose IM, slow IV, SC Q4 hr**Neonatal opiate withdrawal:** 0.08–0.2 mg/dose PO Q3–4 hr PRN**Infant 1–6 mo:****PO:** 0.08–0.1 mg/kg/dose Q3–4 hr PRN**IV:** 0.025–0.03 mg/kg/dose Q2–4 hr PRN**Infant > 6 mo and child:****PO:** 0.2–0.5 mg/kg/dose (**initial max. dose:** 15–20 mg/dose) Q4–6 hr PRN (immediate release) or 0.3–0.6 mg/kg/dose Q12 hr PRN (controlled release)**IM/IV/SC:** 0.1–0.2 mg/kg/dose Q2–4 hr PRN; **max. initial dose:** infant: 2 mg/dose; 1–6 yr: 4 mg/dose; 7–12 yr: 8 mg/dose; adolescent: 10 mg/dose**Adult:****PO:** 10–30 mg Q4 hr PRN (immediate release) or 15–30 mg Q8–12 hr PRN (controlled release)**IM/IV/SQ:** 2–15 mg/dose Q2–6 hr PRN**Continuous IV infusion and SC infusion:** Dosing ranges, titrate to effect.**Neonate (IV route only):** 0.01–0.02 mg/kg/hr**Infant and child:****Postoperative pain:** 0.01–0.04 mg/kg/hr**Sickle cell and cancer:** 0.04–0.07 mg/kg/hr**Adult:** 0.8–10 mg/hr**To prepare infusion for neonates, infants, and children, use the following formula:**

$$50 \times \frac{\text{Desired dose (mg/kg/hr)}}{\text{Desired infusion rate (mL/hr)}} \times \text{Wt (kg)} = \frac{\text{mg Morphine}}{50 \text{ mL Fluid}}$$

Dependence, CNS and respiratory depression, nausea, vomiting, urinary retention, constipation, hypotension, bradycardia, increased ICP, miosis, biliary spasm, and allergy may occur.

**Naloxone may be used to reverse effects, especially respiratory depression.** Causes histamine release, resulting in itching and possible bronchospasm. Low-dose naloxone infusion may be used for itching. Inflammatory masses (e.g., granulomas) have been reported with continuous infusions via indwelling intrathecal catheters.

See Chapter 6 for equianalgesic dosing. Pregnancy category changes to "D" if used for prolonged periods or in higher doses at term. Rectal dosing is same as oral dosing but is not recommended owing to poor absorption.



MORPHINE SULFATE *continued*

The FDA has recently announced safety labeling changes and postmarket study requirements for extended-release/long-acting opioid analgesics; see [www.fda.gov/drugs/drugsafety](http://www.fda.gov/drugs/drugsafety) for updated information. Controlled/sustained-release oral tablets must be administered whole. Controlled-release oral capsules may be opened and the entire contents sprinkled on applesauce immediately before ingestion. Be aware of the various oral solution concentrations; the concentrated oral solution (100 mg/5 mL) has been associated with accidental overdoses. **Adjust dose in renal failure (see Chapter 31).**

**MUIROICIN**

Bactroban, Bactroban Nasal, and generics

**Topical antibiotic**

No



No



2



B

**Ointment:** 2% (22, 30 g); contains polyethylene glycol**Cream:** 2% (15, 30 g); contains benzyl alcohol**Nasal ointment (Bactroban Nasal):** 2% (1 g), as calcium salt**Topical (see remarks):**

≥3 **mo–adult:** Apply small amount TID to affected area × 5–14 days. Topical ointment may be used in infants ≥2 mo for impetigo.

**Intranasal (all ages; see remarks):** Apply small amount intranasally BID × 5–10 days.

**Avoid** contact with eyes. Topical cream is **not** intended for use in lesions >10 cm in length or 100 cm<sup>2</sup> in surface area. **Do not use** topical ointment preparation on open wounds because of concerns about systemic absorption of polyethylene glycol. May cause minor local irritation and dry skin. Intranasal route may cause nasal stinging, taste disorder, headache, rhinitis, and pharyngitis.

If clinical response is not apparent in 3–5 days with topical use, reevaluate infection. Intranasal administration may be used to eliminate carriage of *Staphylococcus aureus*, including MRSA.

**MYCOPHENOLATE**

Mycophenolate mofetil: CellCept and generics

Mycophenolate sodium: Myfortic and generics

**Immunosuppressant agent**

No



Yes



3



D

**Mycophenolate mofetil:****Caps:** 250 mg**Tabs:** 500 mg**Oral suspension:** 200 mg/mL (160 mL); contains phenylalanine (0.56 mg/mL) and methylparabens**Injection:** 500 mg**Mycophenolate sodium:****Tabs:** 500 mg**Delayed-release tabs (Myfortic):** 180, 360 mg**Child (see remarks):****Renal transplant:**

**Caps, tabs, or suspension:** 600 mg/m<sup>2</sup>/dose PO/IV BID up to a **max. dose** of 2000 mg/24 hr. Alternatively, patients with BSAs ≥1.25 m<sup>2</sup> may be dosed as follows:

**1.25–1.5 m<sup>2</sup>:** 750 mg PO BID

**>1.5 m<sup>2</sup>:** 1000 mg PO BID

*Continued*

MYCOPHENOLATE *continued***Child (see remarks):****Renal transplant:**

**Delayed-release tabs (Myfortic):** 400–450 mg/m<sup>2</sup>/dose PO BID. **Max. dose:** 720 mg BID. This dosage form not recommended in patients with BSAs <1.19 m<sup>2</sup>. Alternatively, patients with BSA ≥1.19 m<sup>2</sup> may be dosed as follows:

**1.19–1.58 m<sup>2</sup>:** 540 mg PO BID

**>1.58 m<sup>2</sup>:** 720 mg PO BID

**Nephrotic syndrome:**

**Frequently relapsing:** 12.5–18 mg/kg/dose PO BID up to a **max. dose** of 2000 mg/24 hr for 1–2 years, and taper prednisone regimen.

**Steroid dependent:** 12–18 mg/kg/dose or 600 mg/m<sup>2</sup>/dose PO BID up to a **max. dose** of 2000 mg/24hr.

**Adult (in combination with corticosteroids and cyclosporine; check specific transplantation protocol for specific dosage):**

**IV:** 2000–3000 mg/24 hr ÷ BID

**Oral:**

**Caps, tabs, or suspension:** 2000–3000 mg/24 hr PO ÷ BID

**Delayed-release tabs (Myfortic):** 720–1080 mg PO BID

Check specific transplantation protocol for specific dosage. Mycophenolate mofetil is a prodrug for mycophenolic acid. Owing to differences in absorption, delayed-release tablets should **not** be interchanged with other oral dosage forms on an equivalent mg-to-mg basis. Increases risk of first-trimester pregnancy loss and increased risk of congenital malformations (especially external ear and facial abnormalities [e.g., cleft lip and palate] and anomalies of distal limbs, heart, and esophagus).

Common side effects may include headache, hypertension, diarrhea, vomiting, bone marrow suppression, anemia, fever, opportunistic infections, and sepsis. May increase risk for bacterial, fungal, protozoal, and viral infections, and lymphomas or other malignancies. GI bleeds and increased risk for rejection in heart transplant patients switched from calcineurin inhibitors (e.g., cyclosporine, tacrolimus) and CellCept to sirolimus and CellCept have been reported. Cases of progressive multifocal leukoencephalopathy (PML) and pure red cell aplasia (PRCA) have also been reported.

**Use with caution** in patients with active GI disease or renal impairment (GFR < 25 mL/min/1.73 m<sup>2</sup>) outside of the immediate posttransplant period. In adults with renal impairment, **avoid** doses >2 g/24 hr and observe carefully. Dose should be interrupted or reduced in the presence of neutropenia (ANC < 1.3 × 10<sup>3</sup>/μL). No dose adjustment is needed for patients experiencing delayed graft function postoperatively.

**Drug interactions:** (1) Displacement of phenytoin or theophylline from protein binding sites will decrease total serum levels and increase free serum levels of these drugs. Salicylates displace mycophenolate to increase free levels of mycophenolate. (2) Competition for renal tubular secretion results in increased serum levels of acyclovir, ganciclovir, probenecid, and mycophenolate (when any of these are used together). (3) **Avoid** live and live attenuated vaccines (including influenza); decreases vaccine effectiveness. (4) Proton-pump inhibitors may reduce mycophenolate levels.

Administer oral doses on an empty stomach. Cholestyramine and antacid use may decrease mycophenolic acid levels. Infuse IV doses over 2 hr. Oral suspension may be administered via NG tube with a minimum size of 8 French.



**NAFCILLIN**

Nallpen and generics

**Antibiotic, penicillin (penicillinase resistant)**

Yes



Yes



2



B

**Injection:** 1, 2, 10 g; contains 2.9 mEq Na/g drug**Injection, premixed in iso-osmotic dextrose:** 1 g in 50 mL, 2 g in 100 mL**Neonate (IM/IV):****≤7 days:**

&lt;2 kg: 50 mg/kg/24 hr ÷ Q12 hr

≥2 kg: 75 mg/kg/24 hr ÷ Q8 hr

**>7 days:**

&lt;1.2 kg: 50 mg/kg/24 hr ÷ Q12 hr

1.2–2 kg: 75 mg/kg/24 hr ÷ Q8 hr

≥2 kg: 100 mg/kg/24 hr ÷ Q6 hr

**Infant and child (IM/IV):****Mild to moderate infections:** 50–100 mg/kg/24 hr ÷ Q6 hr**Severe infections:** 100–200 mg/kg/24 hr ÷ Q4–6 hr; give 200 mg/kg/24 hr ÷ Q4–6 hr for staphylococcal endocarditis**Max. dose:** 12 g/24 hr**Adult:****IV:** 500–2000 mg Q4–6 hr**IM:** 500 mg Q4–6 hr**Max. dose:** 12 g/24 hr

Allergic cross-sensitivity with penicillin. **Oral route not recommended because of unpredictable absorption.** Solutions containing dextrose may be **contraindicated** in patients with known allergy to corn or corn products. High incidence of phlebitis with IV dosing. CSF penetration is poor unless meninges are inflamed. **Use with caution** in patients with combined renal and hepatic impairment (reduce dose by 33%–50%). Nafcillin may increase elimination of cyclosporine and warfarin. Acute interstitial nephritis is rare. May cause rash, bone marrow suppression, and false-positive urinary and serum proteins. Hypokalemia has been reported.

**NALOXONE**

Narcan and many generics

**Narcotic antagonist**

No



No



?



C

**Injection:** 0.4 mg/mL (1, 10 mL); some preparations may contain parabens**Injection, in syringe:** 1 mg/mL (2 mL)**Opiate intoxication (IM/IV/SC, use 2–10 times IV dose for ETT route; see remarks):****Neonate, infant, child ≤ 20 kg or ≤ 5 yr:** 0.1 mg/kg/dose. May repeat PRN Q2–3 min.**Child > 20 kg or > 5 yr:** 2 mg/dose. May repeat PRN Q2–3 min.**Continuous infusion (child and adult):** 0.005 mg/kg loading dose, followed by infusion of 0.0025 mg/kg/hr has been recommended. A range of 0.0025–0.16 mg/kg/hr has been reported. Taper gradually to avoid relapse.**Adult:** 0.4–2 mg/dose. May repeat PRN Q2–3 min. Use 0.1- to 0.2-mg increments in opiate-dependent patients.

Continued

NALOXONE *continued*

**Opiate-induced pruritus (limited data):** 0.25–2 mcg/kg/hr IV; a dose-finding study in 59 children suggests a minimum dose of 1 mcg/kg/hr when used as prophylactic therapy. Doses  $\geq 3$  mcg/kg/hr increase risk for reduced pain control.

Short duration of action may necessitate multiple doses. For severe intoxication, doses of 0.2 mg/kg may be required. If no response is achieved after a cumulative dose of 10 mg, reevaluate diagnosis. **In the nonarrest situation, use lowest dose effective (may start at 0.001 mg/kg/dose). See Chapter 6 for additional information.**

Will produce narcotic withdrawal syndrome in patients with chronic dependence. **Use with caution** in patients with chronic cardiac disease. Abrupt reversal of narcotic depression may result in nausea, vomiting, diaphoresis, tachycardia, hypertension, and tremulousness.

IV administration preferred. Onset of action may be delayed with other routes of administration.

**NAPROXEN/NAPROXEN SODIUM**

Naprosyn, Anaprox, EC-Naprosyn, Naprosyn DR, Naprelan, Aleve [OTC], and many others

**Nonsteroidal antiinflammatory agent**



Yes



Yes



3



C/D

**Naproxen:**

**Tablets (Naprosyn and generics):** 250, 375, 500 mg

**Delayed-release tablets (EC-Naprosyn, Naprosyn DR):** 375, 500 mg

**Oral suspension:** 125 mg/5 mL; contains 0.34 mEq Na/1 mL and parabens

**Naproxen Sodium:****Tablets:**

Aleve and others [OTC]: 220 mg (200 mg base); contains 0.87 mEq Na

Anaprox and generics: 275 mg (250 mg base), 550 mg (500 mg base); contains 1 mEq, 2 mEq Na, respectively

**Controlled-release tablets (Naprelan):** 412.5 mg (375 mg base), 550 mg (500 mg base), 825 mg (750 mg base)

**All doses based on naproxen base.**

**Child > 2 yr:**

**Analgesia:** 5–7 mg/kg/dose Q8–12 hr PO

**JRA:** 10–20 mg/kg/24 hr  $\div$  Q12 hr PO

**Usual max. dose:** 1000 mg/24 hr

**Adult:**

**Analgesia (includes adolescents):**

**Over-the-counter dosage forms:** 200 mg Q8–12 hr PRN PO; if needed, 400 mg initial dose may be needed. **Max. dose:** 600 mg/24 hr.

**Prescription-strength dosage forms:** 250 mg Q8–12 hr PRN (500 mg initial dose may be needed) **OR** 500 mg Q12 hr PRN PO. **Max. dose:** 1250 mg/24 hr for first day then 1000 mg/24 hr.

**Rheumatoid arthritis, ankylosing spondylitis:**

**Immediate-release forms:** 250–500 mg BID PO

**Delayed-release tablets (EC-Naprosyn, Naprosyn DR):** 375–500 mg BID PO

**Controlled-release tablets (Naprelan):** 750–1000 mg once daily PO. For patients converting from immediate and delayed-release forms, calculate daily dose and administer Naprelan as a single daily dose.

**Max. dose (all dosage forms):** 1500 mg/24 hr



NAPROXEN/NAPROXEN SODIUM *continued***Dysmenorrhea (adult):**

500 mg  $\times$  1, then 250 mg Q6–8 hr PRN PO or 500 mg Q12 hr PRN PO; **max. dose:** 1250 mg/24 hr for first day, then 1000 mg/24 hr

**Contraindicated** in treating perioperative pain for coronary artery bypass graft surgery. May cause GI bleeding, thrombocytopenia, heartburn, headache, drowsiness, vertigo, and tinnitus.

**Use with caution** in patients with GI disease, cardiac disease (risk for thrombotic events, MI, stroke), renal or hepatic impairment, and those receiving anticoagulants. See *Ibuprofen* for other side effects.

Pregnancy category changes to "D" if used in the third trimester or near delivery. Administer doses with food or milk to reduce GI discomfort.

**NEOMYCIN SULFATE**

Neo-fradin and generics

**Antibiotic, aminoglycoside; ammonium detoxicant**



No



Yes



?



D

**Tabs:** 500 mg

**Oral solution (Neo-Fradin):** 125 mg/5 mL (480 mL); contains parabens

**Diarrhea:**

**Preterm and newborn:** 50 mg/kg/24 hr  $\div$  Q6 hr PO

**Hepatic encephalopathy:**

**Infant and child:** 50–100 mg/kg/24 hr  $\div$  Q6–8 hr PO  $\times$  5–6 days; **max. dose:** 12 g/24 hr

**Adult:** 4–12 g/24 hr  $\div$  Q4–6 hr PO  $\times$  5–6 days

**Bowel prep (in combination with erythromycin base):**

**Child:** 90 mg/kg/24 hr PO  $\div$  Q4 hr  $\times$  2–3 days

**Adult:** 1 g Q1 hr PO  $\times$  4 doses, then 1 g Q4 hr PO  $\times$  5 doses; many other regimens exist.

**Contraindicated** in ulcerative bowel disease, intestinal obstruction, or aminoglycoside hypersensitivity. Monitor for nephrotoxicity and ototoxicity. Oral absorption is limited, but levels may accumulate. Consider dosage reduction in the presence of renal failure. May cause itching, redness, edema, colitis, candidiasis, or poor wound healing if applied topically. Prevalence of neomycin hypersensitivity has increased. May decrease absorption of penicillin V, vitamin B<sub>12</sub>, digoxin, and methotrexate. May potentiate oral anticoagulants and adverse effects of other neurotoxic, ototoxic, or nephrotoxic drugs.

**NEOMYCIN/POLYMYXIN B  $\pm$  BACITRACIN****NEOMYCIN/POLYMYXIN B:**

Neosporin GU Irrigant

**NEOMYCIN/POLYMYXIN B + BACITRACIN:**

Neosporin, Neo To Go, Neo-Polycin, Neosporin Ophthalmic, and generics

**Topical antibiotic**



No



No



?



C/D

**NEOMYCIN/POLYMYXIN B:**

**Solution, genitourinary irrigant:** 40 mg neomycin sulfate, 200,000 U polymyxin B/mL (1, 20 mL); multidose vial contains methylparabens.

*Continued*



NEOMYCIN/POLYMYXIN B/± BACITRACIN *continued***NEOMYCIN/POLYMYXIN B + BACITRACIN:**

**Ointment, topical (Neosporin, Neo To Go) [OTC]:** 3.5 mg neomycin sulfate, 400 U bacitracin, 5000 U polymyxin B/g (0.9, 15, 30, 454 g)

**Ointment, ophthalmic (Neosporin Ophthalmic):** 3.5 mg neomycin sulfate, 400 U bacitracin, 10,000 U polymyxin B/g (3.5 g)

**NEOMYCIN/POLYMYXIN B + BACITRACIN:****Child and adult:**

**Topical:** Apply to minor wounds and burns once–twice daily

**Ophthalmic:** Apply small amount to conjunctiva Q3–4 hr × 7–10 days, depending on severity of infection.

**NEOMYCIN/POLYMYXIN B:****Bladder irrigation:**

**Child and adult:** Mix 1 mL in 1000 mL NS and administer via a three-way catheter at a rate adjusted to patient's urine output. Do not exceed 10 days of continuous use.

**Do not use** for extended periods. May cause superinfection, delayed healing. See *Neomycin* for additional remarks. Ophthalmic preparation may cause stinging and sensitivity to bright light. **Avoid** use of bladder irrigant in patients with defects in the bladder mucosa or wall. Prevalence of neomycin hypersensitivity has increased.

Pregnancy category is a "C" for neomycin/polymyxin B/bacitracin and a "D" for neomycin/polymyxin B.

**NEOSTIGMINE**

Prostigmin, Bioxiverz, and generics

**Anticholinesterase (cholinergic) agent**



No



Yes



2



C

**Tabs:** 15 mg (bromide)

**Injection:** 0.5, 1 mg/mL (methylsulfate); may contain parabens or phenol

**Myasthenia gravis diagnosis:** Use with atropine (see remarks).

**Child:** 0.025–0.04 mg/kg IM × 1

**Adult:** 0.02 mg/kg IM × 1

**Treatment:****Child:**

**IM/IV/SC:** 0.01–0.04 mg/kg/dose Q2–4 hr PRN

**PO:** 2 mg/kg/24 hr ÷ Q3–4 hr; **max. dose:** 375 mg/24 hr

**Adult:**

**IM/IV/SC:** 0.5–2.5 mg/dose Q1–3 hr PRN up to **max. dose** of 10 mg/24 hr

**PO:** Start with 15 mg/dose TID. May increase every 1–2 days. Dosage requirements may vary from 15–375 mg/24 hr with an average of 150 mg/24 hr. Some patients may require as much as 30–40 mg Q2–4 hr.

**Reversal of nondepolarizing neuromuscular blocking agents:** Administer with atropine or glycopyrrolate.

**Infant:** 0.025–0.1 mg/kg/dose IV

**Child:** 0.025–0.08 mg/kg/dose IV

**Adult:** 0.5–2.5 mg/dose IV

**Max. dose (all ages):** 5 mg/dose

NEOSTIGMINE *continued*

**Contraindicated** in GI and urinary obstruction. **Caution** in asthmatics. May cause cholinergic crisis, bronchospasm, salivation, nausea, vomiting, diarrhea, miosis, diaphoresis, lacrimation, bradycardia, hypotension, fatigue, confusion, respiratory depression, and seizures. Titrate for each patient, but **avoid** excessive cholinergic effects.



For diagnosis of myasthenia gravis (MG), administer atropine 0.011 mg/kg/dose IV immediately before or IM (0.011 mg/kg/dose) 30 min before neostigmine. For treatment of MG, patients may need higher doses of neostigmine at times of greatest fatigue.

**Antidote:** Atropine 0.01–0.04 mg/kg/dose. Atropine and epinephrine should be available in the event of a hypersensitivity reaction.

**Adjust dose in renal failure (see Chapter 31).**

## NEVIRAPINE

Viramune, Viramune XR, NVP, and generics

**Antiviral, non-nucleoside reverse transcriptase inhibitor**



Yes



Yes



3



B

**Tabs:** 200 mg

**Extended-release tabs (Viramune XR):** 400 mg

**Oral suspension:** 10 mg/mL (240 mL); contains parabens

**HIV:** See [www.aidsinfo.nih.gov/guidelines](http://www.aidsinfo.nih.gov/guidelines)



**Prevention of vertical transmission during high-risk situations (women who received no antepartum antiretroviral prophylaxis, women with suboptimal viral suppression at delivery, or women with known antiretroviral drug-resistant virus) and in combination with zidovudine (see Chapter 17 for additional information):**

**Newborn:** 3 doses (based on birth weight) in the first week of life; dose 1: within 0–48 hr of birth; dose 2: 48 hr after dose 1; dose 3: 96 hr after dose 2

**Birth weight 1.5–2 kg:** 8 mg/dose PO

**Birth weight > 2 kg:** 12 mg/dose PO

See [www.aidsinfo.nih.gov/guidelines](http://www.aidsinfo.nih.gov/guidelines) for additional remarks.



**Use with caution** in patients with hepatic or renal dysfunction. **Contraindicated** in moderate/severe hepatic impairment (Child-Pugh Class B or C) and postexposure (occupational or non-occupational) prophylaxis regimens. Most frequent side effects include: rash (may be life-threatening, including Stevens-Johnson syndrome; permanently discontinue and never restart), fever, abnormal liver function tests, headache, and nausea. **Discontinue therapy** if any of the following occurs: severe rash; rash with fever, blistering, oral lesions, conjunctivitis, or muscle aches. Permanently discontinue and do not restart therapy if symptomatic hepatitis, severe transaminase elevations, or hypersensitivity reactions occur.

**Life-threatening** hepatotoxicity has been reported, primarily during first 12 wk of therapy. Patients with increased serum transaminase or history of hepatitis B or C infection before nevirapine are at greater risk for hepatotoxicity. Women, including pregnant women, with CD4 counts >250 cells/mm<sup>3</sup> or men with CD4 counts >400 cells/mm<sup>3</sup> are at risk for hepatotoxicity. Monitor liver function tests (obtain transaminases immediately after development of hepatitis signs/symptoms, hypersensitivity reactions, or rash) and CBCs. Hypophosphatemia has been reported.

Nevirapine induces the CYP 450 3A4 drug-metabolizing isoenzyme to cause an autoinduction of its own metabolism within the first 2–4 wk of therapy and has the potential to interact with many drugs.

**Carefully review patients' drug profile for other drug interactions each time nevirapine is initiated or when a new drug is added to a regimen containing nevirapine.**

Doses can be administered with food and concurrently with didanosine.

**NIACIN/VITAMIN B<sub>3</sub>**

Niacor, Niaspan, Slo-Niacin, Nicotinic acid, Vitamin B<sub>3</sub>, and many generics

*Vitamin, water soluble*



Yes



Yes



?



A/C

**Tabs [OTC]:** 50, 100, 250, 500 mg

**Timed or extended-release tabs [all OTC except 1000 mg]:** 250, 500, 750, 1000 mg

**Timed or extended-release caps [OTC]:** 250, 500 mg

**US RDA:** See Chapter 21.

**Pellagra (PO):**

**Child:** 50–100 mg/dose TID

**Adult:** 50–100 mg/dose TID–QID

**Max. dose:** 500 mg/24 hr



**Contraindicated** in hepatic dysfunction, active peptic ulcer, and severe hypotension. Use with caution in unstable angina, acute MI (especially if receiving vasoactive drugs), renal dysfunction, and in patients with history of jaundice, hepatobiliary disease, or peptic ulcer. Adverse reactions of flushing, pruritus, or GI distress may occur with PO administration. May cause hyperglycemia, hyperuricemia, blurred vision, abnormal liver function tests, dizziness, and headaches. Burning sensation of the skin, skin discoloration, hepatitis, and elevated creatine kinase have been reported. May cause false-positive urine catecholamines (fluorometric methods) and urine glucose (Benedict's reagent).



Pregnancy category changes to "C" if used in doses above the RDA or for typical doses used for lipid disorders. **See Chapter 21 for multivitamin preparations.**

**NICARDIPINE**

Cardene IV, Cardene SR, and generics

*Calcium channel blocker, antihypertensive*



Yes



Yes



2



C

**Caps (immediate-release):** 20, 30 mg

**Sustained-release caps (Cardene SR):** 30, 60 mg

**Injection (Cardene IV):** 0.1 mg/mL (200 mL), 0.2 mg/mL (200 mL), 2.5 mg/mL (10 mL; also available in generic)

**Child (see remarks):**

**Hypertension:**

**Continuous IV infusion:** Start at 0.5–1 mcg/kg/min; dose may be increased as needed every 15–30 min up to a **max.** of 4–5 mcg/kg/min.

**Adult:**

**Hypertension:**

**Oral:**

**Immediate release:** 20 mg PO TID; dose may be increased after 3 days to 40 mg PO TID if needed.

**Sustained release:** 30 mg PO BID; dose may be increased after 3 days to 60 mg PO BID if needed.

**Continuous IV infusion:** Start at 5 mg/hr; increase dose as needed by 2.5 mg/hr Q5–15 min up to a **max. dose** of 15 mg/hr. After attainment of desired BP, decrease infusion to 3 mg/hr and adjust rate as needed to maintain desired response.



NICARDIPINE *continued*

Reported use in children has been limited to a small number preterm infants, infants, and children. **Contraindicated** in advanced aortic stenosis. **Avoid** systemic hypotension in patients after an acute cerebral infarct or hemorrhage. **Use with caution** in hepatic or renal dysfunction by carefully titrating dose. The drug undergoes significant first-pass metabolism through the liver and is excreted in the urine (60%).

May cause headache, dizziness, asthenia, peripheral edema, and GI symptoms. Cimetidine increases effects/toxicity of nicardipine. **See Nifedipine for additional drug and food interactions.**

Onset of action for PO administration is 20 min, with peak effects in 0.5–2 hr. IV onset of action is 1 min. Duration of action after a single IV or PO dose is 3 hr. To reduce risk for venous thrombosis, phlebitis, and vascular impairment with IV administration, do not use small veins (e.g., dorsum of hand or wrist). Avoid intraarterial administration or extravasation. For additional information, see Chapter 4.

**NIFEDIPINE**

Adalat CC, Nifediac CC, Procardia, Procardia XL, and many generics

**Calcium channel blocker, antihypertensive**



No



No




2



C

**Caps (Procardia and generics):** 10 mg (0.34 mL), 20 mg (0.45 mL)

**Sustained-release tabs (Adalat CC, Nifediac CC, Procardia XL, and others):** 30, 60, 90 mg

**Oral suspension:** 1, 4 mg/mL 

**Child (see remarks for precautions):**

**Hypertensive urgency:** 0.1–0.25 mg/kg/dose Q4–6 hr PRN PO/SL; **max. dose:** 10 mg/dose or 1–2 mg/kg/24 hr

**Hypertension:**

**Sustained-release tabs:** Start with 0.25–0.5 mg/kg/24 hr (**max. dose:** 30–60 mg/24 hr) ÷ Q12–24 hr. May increase to **max. dose** of 3 mg/kg/24 hr up to 120 mg/24 hr.

**Hypertrophic cardiomyopathy (infant):** 0.6–0.9 mg/kg/24 hr ÷ Q6–8 hr PO/SL

**Adult:****Hypertension:**

**Sustained-release tabs:** Start with 30 mg PO once daily; usual range: 30–60 mg once daily. May increase to **max. dose** of 90 mg/24 hr for Adalat CC and 120 mg/24 hr for Procardia XL.

**Angina:**

**Caps:** Start with 10 mg/dose PO TID. May increase to 30 mg/dose PO TID–QID. **Max. dose:** 180 mg/24 hr.

Use of immediate-release dosage form in children is controversial and has been abandoned by some. **Use with caution** in children with acute CNS injury, owing to increased risk for stroke, seizure, and altered level of consciousness. To prevent rapid decrease in blood pressure in children, an initial dose of  $\leq 0.25$  mg/kg is recommended.

**Use with caution** in patients with CHF, aortic stenosis, GI obstruction/narrowing (bezoar formation), and cirrhosis (reduced drug clearance). May cause severe hypotension, peripheral edema, flushing, tachycardia, headaches, dizziness, nausea, palpitations, and syncope. Acute generalized exanthematous pustulosis has been reported.

Although overall use in adults has been abandoned, the immediate-release dosage form is **contraindicated** in adults with severe obstructive coronary artery disease or recent MI, and in hypertensive emergencies.

*Continued*

NIFEDIPINE *continued*

Nifedipine is a substrate for CYP 450 3A3/4 and 3A5–7. **Do not administer** with grapefruit juice; may increase bioavailability and effects. Itraconazole and ketoconazole may increase nifedipine levels/effects. CYP 3A inducers (e.g., rifampin, rifabutin, phenobarbital, phenytoin, carbamazepine) may reduce nifedipine's effects. Nifedipine may increase phenytoin, cyclosporine, and digoxin levels. For hypertensive emergencies, **see Chapter 4**.

For sublingual administration, capsule must be punctured and liquid expressed into mouth. A small amount is absorbed via the SL route. Most effects are due to swallowing and oral absorption. **Do not** crush or chew sustained-release tablet dosage form.

**NITROFURANTOIN**

Furadantin, Macrochantin, Macrobid, and generics

**Antibiotic**



Yes



Yes



2



B/X

**Caps (macrocrystals; Macrochantin and generics):** 25, 50, 100 mg

**Caps (dual-release; Macrobid):** 100 mg (25 mg macrocrystal/75 mg monohydrate)

**Oral suspension (Furadantin and generics):** 25 mg/5 mL (230 mL); contains parabens and saccharin

**Child (>1 mo; oral suspension or macrocrystals):**

**Treatment:** 5–7 mg/kg/24 hr ÷ Q6 hr PO; **max. dose:** 400 mg/24 hr

**UTI prophylaxis:** 1–2 mg/kg/dose QHS PO; **max. dose:** 100 mg/24 hr

**≥ 12 yr and adult:**

**Macrocrystals:** 50–100 mg/dose Q6 hr PO

**Dual-release (Macrobid):** 100 mg/dose Q12 hr PO

**UTI prophylaxis (macrocrystals):** 50–100 mg/dose PO QHS



**Contraindicated** in severe renal disease, infants <1 mo of age, GFR <60 mL/min (reduced drug distribution the urine), active/previous cholestatic jaundice/hepatic dysfunction, and pregnant women at term. **Use with caution** in G6PD deficiency, anemia, lung disease, and peripheral neuropathy. May cause nausea, hypersensitivity reactions (including vasculitis), vomiting, cholestatic jaundice, headache, hepatotoxicity, polyneuropathy, and hemolytic anemia.



Anticholinergic drugs and high-dose probenecid may increase nitrofurantoin toxicity. Magnesium salts may decrease nitrofurantoin absorption. Causes false-positive urine glucose with Clinitest.

Administer doses with food or milk.

Pregnancy category changes to "X" at term (38–42 wk' gestation). Breast-feeding in mothers receiving nitrofurantoin is not recommended for infants <1 and those with G6PD deficiency; use in infants ≥1 mo and without G6PD deficiency is compatible.

**NITROGLYCERIN**

Nitro-Bid, Nitrostat, Nitro-Time, Nitro-Dur, NitroMist, and many others

**Vasodilator, antihypertensive**



Yes



Yes



?



C

**Injection:** 5 mg/mL (10 mL); may contain alcohol or propylene glycol

**Prediluted injection in D<sub>5</sub>W:** 100 mcg/mL, 200 mcg/mL, 400 mcg/mL (250, 500 mL)

**Sublingual tabs (Nitrostat and others):** 0.3, 0.4, 0.6 mg

**Sustained-release caps (Nitro-Time and others):** 2.5, 6.5, 9 mg

**Ointment, topical (Nitro-Bid):** 2% (1, 30, 60 g)

NITROGLYCERIN *continued*

**Patch (Nitro-Dur and others):** 2.5 mg/24 hr (0.1 mg/hr), 5 mg/24 hr (0.2 mg/hr), 7.5 mg/24 hr (0.3 mg/hr), 10 mg/24 hr (0.4 mg/hr), 15 mg/24 hr (0.6 mg/hr), 20 mg/24 hr (0.8 mg/hr)

**Spray, translingual (NitroMist and others):** 0.4 mg per metered spray (4.1, 8.5 g; delivers 90 and 230 doses, respectively); contains butane (flammable)

**NOTE:** The IV dosage units for children are in mcg/kg/min, compared with mcg/min for adults.

**Child:**

**Continuous IV infusion:** Begin with 0.25–0.5 mcg/kg/min; may increase by 0.5–1 mcg/kg/min Q3–5 min PRN. Usual dose: 1–5 mcg/kg/min. **Max. dose:** 20 mcg/kg/min.

**Adult:**

**Continuous IV infusion:** 5 mcg/min IV, then increase Q3–5 min PRN by 5 mcg/min up to 20 mcg/min. If no response, increase by 10 mcg/min Q3–5 min PRN up to a **max.** of 400 mcg/min.

**Sublingual:** 0.2–0.6 mg Q5 min; **max.** of three doses in 15 min

**Oral:** 2.5–9 mg BID–TID; up to 26 mg QID

**Ointment:** Apply 1–2 inches Q8 hr, up to 4–5 inches Q4 hr.

**Patch:** 0.2–0.4 mg/hr initially, then titrate to 0.4–0.8 mg/hr. Apply new patch daily (tolerance is minimized by removing patch for 10–12 hr/24 hr).

**Contraindicated** in glaucoma, severe anemia, and concurrent phosphodiesterase-5 inhibitor (e.g., sildenafil). In small doses (1–2 mcg/kg/min) acts mainly on systemic veins and decreases preload. At 3–5 mcg/kg/min acts on systemic arterioles to decrease resistance. May cause headache, flushing, GI upset, blurred vision, and methemoglobinemia. **Use with caution** in severe renal impairment, increased ICP, and hepatic failure. IV nitroglycerin may antagonize anticoagulant effect of heparin.

Decrease dose gradually in patients receiving drug for prolonged periods to **avoid** withdrawal reaction. Must use polypropylene infusion sets to **avoid** adsorption of drug to plastic tubing. Use in heparinized patients may result in a decrease of PTT, with subsequent rebound effect upon discontinuation of nitroglycerin.

Onset (duration) of action: IV: 1–2 min (3–5 min); sublingual: 1–3 min (30–60 min); PO sustained release: 40 min (4–8 hr); topical ointment: 20–60 min (2–12 hr); and transdermal patch: 40–60 min (18–24 hr).

**NITROPRUSSIDE**

Nitropress (previously available as Nipride)

**Vasodilator, antihypertensive**



Yes



Yes



?



C

**Injection:** 25 mg/mL (2 mL)

**Child and adult:** IV, continuous infusion

**Dose:** Start at 0.3–0.5 mcg/kg/min, titrate to effect. Usual dose is 3–4 mcg/kg/min.

**Max. dose:** 8–10 mcg/kg/min

**Contraindicated** in patients with decreased cerebral perfusion and in situations of compensatory hypertension (increased ICP). Monitor for hypotension and acidosis. Dilute with D<sub>5</sub>W and protect from light.

Nitroprusside is nonenzymatically converted to cyanide, which is converted to thiocyanate. Cyanide may produce metabolic acidosis and methemoglobinemia; thiocyanate may produce psychosis and seizures. Monitor thiocyanate levels if used for >48 hr or if dose ≥ 4 mcg/kg/min. **Thiocyanate levels should be <50 mg/L.** Monitor **cyanide levels (toxic levels > 2 mcg/mL)** in patients with hepatic dysfunction and thiocyanate levels in patients with renal dysfunction.

Onset of action is 2 min, with a 1- to 10-min duration of effect.

**NOREPINEPHRINE BITARTRATE**

Levophed and generics

**Adrenergic agonist**

No



No



?



C

**Injection:** 1 mg/mL as norepinephrine base (4 mL); contains sulfites**NOTE:** *The dosage units for children are in mcg/kg/min, compared with mcg/min for adults.***Child:** Continuous IV infusion doses as norepinephrine base. Start at 0.05–0.1 mcg/kg/min. Titrate to effect. **Max. dose:** 2 mcg/kg/min.**Adult:** Continuous IV infusion doses as norepinephrine base. Start at 4 mcg/min and titrate to effect. Usual dosage range: 8–12 mcg/min.

May cause cardiac arrhythmias, hypertension, hypersensitivity, headaches, vomiting, uterine contractions, and organ ischemia. May cause decreased renal blood flow and urine output. Avoid extravasation into tissues; may cause severe tissue necrosis. If this occurs, treat locally with phentolamine.

**NORFLOXACIN**

Noroxin

**Antibiotic, quinolone**

No



Yes



2



C

**Tabs:** 400 mg**Oral suspension:** 20 mg/mL **Child:****UTI (limited data in children 5 mo–19 yr [see remarks]):** 9–14 mg/kg/24 hr PO ÷ Q12 hr.**Max. dose:** 800 mg/24 hr. For UTI prophylaxis, give 2–6 mg/kg/24 hr.**Adult:****UTI:** 400 mg PO Q12 hr (× 7–10 days for uncomplicated cases and × 10–21 days for complicated cases)**Prostatitis:** 400 mg PO Q12 hr × 28 days

Like other quinolones, there is concern regarding development of arthropathy. Norfloxacin does **not** adequately treat *Chlamydia* co-infections. UTI dosing can be used for BK virus nephropathy in immunocompromised patients. Fluoroquinolones are no longer recommended for gonorrhea by the CDC owing to resistance. **Use with caution** in children <18 yr, seizures, proarrhythmic conditions, diabetes, patients receiving Class Ia or Class III antiarrhythmics and impaired renal function (**adjust dose in renal failure; see Chapter 31**).

Inhibits CYP 450 1A2. May increase serum cyclosporine and theophylline levels and decrease mycophenolate levels. May prolong PT in patients on warfarin. Nitrofurantoin may decrease norfloxacin's antibacterial effects. Probenecid may increase norfloxacin's effects/toxicity. See *Ciprofloxacin* for common side effects and other drug interactions. QTc prolongation, peripheral neuropathy, and tendon rupture (with all ages, especially with corticosteroid use) have been reported.

**Administer oral doses on an empty stomach.**

**NORTRIPTYLINE HYDROCHLORIDE**

Pamelor and various generics

**Antidepressant, tricyclic**

Yes



No



2



D

**Caps:** 10, 25, 50, 75 mg; may contain benzyl alcohol, EDTA**Oral solution:** 10 mg/5 mL; contains up to 4% alcohol**Depression:****Child 6–12 yr:** 1–3 mg/kg/24 hr ÷ TID–QID PO **OR** 10–20 mg/24 hr ÷ TID–QID PO**Adolescent:** 1–3 mg/kg/24 hr ÷ TID–QID PO **OR** 30–50 mg/24 hr ÷ TID–QID PO**Adult:** 75–100 mg/24 hr ÷ TID–QID PO**Max. dose (all ages):** 150 mg/24 hr**Nocturnal enuresis:****6–7 yr (20–25 kg):** 10 mg PO QHS**8–11 yr (26–35 kg):** 10–20 mg PO QHS**>11 yr (36–54 kg):** 25–35 mg PO QHS

See *Imipramine* for contraindications and common side effects. Also contraindicated with linezolid or IV methylene because of increased risk for serotonin syndrome. Fewer CNS and anticholinergic side effects than amitriptyline. Lower doses and slower dose titration is recommended in hepatic impairment. Therapeutic antidepressant effects occur in 7–21 days. Monitor for clinical worsening of depression and suicidal ideation/behavior after initiation of therapy or after dose changes. **Do not** discontinue abruptly. Nortriptyline is a substrate for the CYP 450 1A2 and 2D6 drug-metabolizing enzymes. Rifampin may increase metabolism of nortriptyline.

**Therapeutic nortriptyline levels for depression:** 50–150 ng/mL. Recommended serum sampling time: obtain a single level 8 or more hr after an oral dose (after 4 days of continuous dosing for children and after 9–10 days for adults).

Administer with food to decrease GI upset.

**NYSTATIN**

Bio-Statín, Mycostatin, Nilstat, and generics

**Antifungal agent**

No



No



1



A/C

**Tabs:** 500,000 U**Caps:** 500,000, 1,000,000 U**Oral suspension:** 100,000 U/mL (5, 60, 480 mL)**Cream/ointment:** 100,000 U/g (15, 30 g)**Topical powder:** 100,000 U/g (15, 30 g)**Vaginal tabs:** 100,000 U (15s)**Oropharyngeal candidiasis:****Preterm infant:** 0.5 mL (50,000 U) to each side of mouth QID**Term infant:** 1 mL (100,000 U) to each side of mouth QID**Child/adult:****Oral suspension:** 4–6 mL (400,000–600,000 U), swish and swallow QID**Vaginal:****Adolescent and adult:** 1 tab QHS × 14 days**Topical:** Apply to affected areas BID–QID.

Continued



NYSTATIN *continued*

May produce diarrhea and GI side effects. Local irritation, contact dermatitis and Stevens-Johnson syndrome have been reported. Treat until 48–72 hr after resolution of symptoms. Drug is poorly absorbed through GI tract. **Do not** swallow troches whole (allow to dissolve slowly). Oral suspension should be swished about the mouth and retained in mouth as long as possible before swallowing.

Pregnancy category is "A" for vaginal product and "C" for oral and topical products.

**OCTREOTIDE ACETATE**

Sandostatin, Sandostatin LAR Depot, and generics  
**Somatostatin analog, antisecretory agent**



No



Yes



?



B

**Injection (amps):** 0.05, 0.1, 0.5 mg/mL (1 mL)

**Injection (multidose vials):** 0.2, 1 mg/mL (5 mL); contains phenol

**Injection, microspheres for suspension (Sandostatin LAR Depot):** 10, 20, 30 mg (in kits with 2 mL diluent and 1.5-inch, 20-gauge needles)

**Infant and child (limited data):****Intractable diarrhea:**

**IV/SC:** 1–10 mcg/kg/24 hr ÷ Q12–24 hr. Dose may be increased within the recommended range by 0.3 mcg/kg/dose Q3 days as needed. **Max. dose:** 1500 mcg/24 hr.

**IV continuous infusion:** 1 mcg/kg/dose bolus, followed by 1 mcg/kg/hr has been used in diarrhea associated with graft-versus-host disease.



Cholelithiasis, hyperglycemia, hypoglycemia, hypothyroidism, nausea, diarrhea, abdominal discomfort, headache, dizziness, and pain at injection site may occur. Growth hormone suppression may occur with long-term use. Bradycardia, thrombocytopenia, and increased risk for pregnancy in patients with acromegaly and pancreatitis have been reported. Cyclosporine levels may be reduced in patients receiving this drug. May increase effects/toxicity of bromocriptine.

Patients with severe renal failure requiring dialysis may require dosage adjustments owing to an increase in half-life. Effects of hepatic dysfunction on octreotide have not been evaluated.

Sandostatin LAR Depot is administered once every 4 wk **only** by the IM route and is currently indicated for use in adults who have been stabilized on IV/SC therapy. See package insert for details.

**OFLOXACIN**

Floxin, Floxin Otic, Ocuflox, and generics  
**Antibiotic, quinolone**



Yes



Yes



2



C

**Otic solution (Floxin Otic and generics):** 0.3% (5, 10 mL)

**Ophthalmic solution (Ocuflox and generics):** 0.3% (5, 10 mL); may contain benzalkonium chloride

**Tabs:** 200, 300, 400 mg

**Otic use:****Otitis externa:**

**6 mo–12 yr:** 5 drops to affected ear(s) once daily × 7 days

**≥13 yr–adult:** 10 drops to affected ear(s) once daily × 7 days

**Chronic suppurative otitis media:**

**≥12 yr–adult:** 10 drops to affected ear(s) BID × 14 days

**Acute otitis media with tympanostomy tubes:**

**1–12 yr:** 5 drops to affected ear(s) BID × 10 days



OFLOXACIN *continued***Ophthalmic use (>1 yr to adult):**

**Conjunctivitis:** 1–2 drops to affected eye(s) Q2–4 hr while awake  $\times$  2 days, then QID for an additional 5 days

**Corneal ulcer:** 1–2 drops to affected eye(s) Q30 min while awake and Q4–6 hr while asleep at night  $\times$  2 days, followed by Q1 hr while awake  $\times$  5 days, and then QID until treatment completed

Pruritus, local irritation, taste perversion, dizziness, earache have been reported with otic use.

Ocular burning/discomfort is frequent with ophthalmic use. Consult with ophthalmology in corneal ulcers.

When using otic solution, warm solution by holding bottle in hand for 1–2 min. Cold solutions may result in dizziness. For otitis externa, patient should lie with affected ear upward before instillation and remain in same position after dose administration for 5 min to enhance drug delivery. For acute otitis media with tympanostomy tubes, patient should lie in same position before instillation, and the tragus should be pumped 4 times after the dose to assist in drug delivery to middle ear.

**For systemic use, adjust dose in severe renal or hepatic impairment (max. dose: 400 mg/24 hr).**

Systemic use of ofloxacin is typically replaced by its S-isomer, levofloxacin, which has a more favorable side-effect profile than ofloxacin. See *Levofloxacin*.

**OLOPATADINE**

Patanol, Pataday, Patanase

**Antihistamine**



No



No



?



C

**Ophthalmic solution:**

**Patanol:** 0.1% (5 mL); contains benzalkonium chloride

**Pataday:** 0.2% (2.5 mL); contains benzalkonium chloride

**Nasal spray (Patanase):** 0.6% (30.5 g provides 240 metered spray doses); contains benzalkonium chloride

**Allergic conjunctivitis:**

**$\geq 3$  yr and adult:**

**0.1% solution (Patanol):** 1 drop in affected eye(s) BID (spaced 6–8 hr apart)

**0.2% solution (Pataday):** 1 drop in affected eye(s) once daily

**Allergic rhinitis:**

**6–11 yr:** Inhale 1 spray into each nostril BID.

**$\geq 12$  yr and adult:** Inhale 2 sprays into each nostril BID.

**Ocular use: DO NOT** use while wearing contact lenses; wait at least 10 min after instilling drops before inserting lenses. Ocular side effects include burning or stinging, dry eye, foreign body sensation, hyperemia, keratitis, lid edema, and pruritus. May also cause headaches, asthenia, pharyngitis, rhinitis, and taste perversion.

**Nasal use:** common side effects include bitter taste and headaches. Nasal ulceration, epistaxis, nasal septal perforation, throat pain and postnasal drip have been reported.

**OLSALAZINE**

Dipentum, Di-mesalazine, Di-5-ASA

**Salicylate, GI anti-inflammatory agent**

Yes



Yes



2



C

**Caps:** 250 mg**Ulcerative colitis:****Child:** Consider using sulfasalazine instead (see remarks).**Adult:** 500 mg PO BID

Drug is converted to 5-aminosalicylic acid (mesalamine) by colonic bacteria; 1 g olsalazine generally delivers 0.9 g of mesalamine to the colon. Only 1%–3% of olsalazine is systemically absorbed.



**Contraindicated** in salicylate hypersensitivity. **Use with caution** in severe liver disease, renal dysfunction, sulfasalazine hypersensitivity, and bronchial asthma. Diarrhea is the most common dose-related side effect. May also cause GI discomfort, headaches, rash, dizziness, and increased risk of bleeding with low-molecular-weight heparins or heparinoids and warfarin. Use with 6-mercaptopurine or thioguanine may increase risk of myelosuppression. Pancreatitis in children and hepatotoxicity have been reported. Monitor urinalysis and renal function.

Administer all doses with food to enhance efficacy.

Use in children (2–18 yr) has been limited to a trial where olsalazine 30 mg/kg/24 hr (**max. dose:** 2 g/24 hr) was found to be less efficacious than sulfasalazine 60 mg/kg/24 hr (**max. dose:** 4 g/24 hr) in treating mild/moderate ulcerative colitis. This may suggest inadequate dosing in this trial; additional studies are needed.

**OMEPRAZOLE**

Prilosec, Prilosec OTC, First-Omeprazole, Omeprazole and Syrspond SF Alka, and generics

In combination with sodium bicarbonate: Zegerid

**Gastric acid pump inhibitor**

Yes




No



2



C

**Caps, sustained-release:** 10, 20, 40 mg**Tab, delayed-release (OTC):** 20 mg**Oral suspension:****First-Omeprazole:** 2 mg/mL (90, 150, 300 mL); contains benzyl alcohol**Omeprazole and Syrspond SF Alka:** 2 mg/mL (100 mL); sugar free and preservative free**Compounded formulation:** 2 mg/mL  contains ≈ 0.5 mEq sodium bicarbonate per 1 mg drug**Granules for oral suspension (Prilosec):** 2.5, 10 mg packets (30s)**In combination with sodium bicarbonate:****Powder for oral suspension (Zegerid):** 20, 40 mg packets (30s); each packet (regardless of strength) contains 1680 mg (20 mEq) sodium bicarbonate**Caps, immediate-release (Zegerid):** 20, 40 mg; each capsule (regardless of strength) contains 1100 mg (13.1 mEq) sodium bicarbonate**Chewable tabs (Zegerid):** 20, 40 mg; each tab (regardless of strength) contains 600 mg (7.1 mEq) sodium bicarbonate and 700 mg magnesium hydroxide**Child (≥1 yr):**

**Esophagitis, GERD, or ulcers:** Start at 1 mg/kg/24 hr PO ÷ once daily–BID (**max. dose:** 20 mg/24 hr). Reported effective range: 0.2–3.5 mg/kg/24 hr. Children 1–6 yr may require higher doses because of enhanced drug clearance.



OMEPRAZOLE *continued***Alternative dosing for patients  $\geq 1$  yr:**

5–&lt;10 kg: 5 mg PO once daily

10–&lt;20 kg: 10 mg PO once daily

 $\geq 20$  kg: 20 mg PO once daily**Adult:****Duodenal ulcer or GERD:** 20 mg/dose PO once daily  $\times$  4–8 wk; may give up to 12 wk for erosive esophagitis**Gastric ulcer:** 40 mg/24 hr PO  $\div$  once daily–BID  $\times$  4–8 wk.**Pathologic hypersecretory conditions:** Start with 60 mg/24 hr PO once daily. If needed, dose may be increased up to 120 mg/24 hr PO  $\div$  TID. Daily doses  $>80$  mg should be administered in divided doses.

Common side effects: Headache, diarrhea, nausea, and vomiting. Allergic reactions including anaphylaxis have been reported. Has been associated with increased risk for *Clostridium difficile*-associated diarrhea.

Drug induces CYP 450 1A2 (decreases theophylline levels) and is also a substrate and inhibitor of CYP 2C19. Increases  $T_{1/2}$  of citalopram, diazepam, phenytoin, and warfarin. May decrease effects of itraconazole, ketoconazole, clopidogrel, iron salts, and ampicillin esters. St. John's wort and rifampin may decrease omeprazole's effects. May be used in combination with clarithromycin and amoxicillin for *Helicobacter pylori* infections.

Bioavailability may be increased with hepatic dysfunction or in patients of Asian descent. Safety and efficacy for GERD in children  $<1$  yr have **not** been established.

Administer all doses before meals. Administer 30 min before sucralfate. Capsules contain enteric-coated granules to ensure bioavailability. **Do not** chew or crush capsule. For doses unable to be divided by 10 mg, capsule may be opened and intact pellets may be administered in an acidic beverage (e.g., apple juice, cranberry juice) or applesauce. The extemporaneously compounded oral suspension product may be less bioavailable owing to loss of enteric coating.

**ONDANSETRON**

Zofran and generics

**Antiemetic agent, 5-HT<sub>3</sub> antagonist**

Yes



No



?



B

**Injection:** 2 mg/mL (2, 20 mL); may contain parabens; some preparations are preservative free.**Tabs:** 4, 8, 24 mg**Tabs, orally disintegrating (ODT):** 4, 8 mg; contains aspartame**Oral solution:** 4 mg/5 mL (50 mL); contains sodium benzoate**Preventing nausea and vomiting associated with chemotherapy:****Oral (give initial dose 30 min before chemotherapy):****Child ( $\geq 2$  yr and adolescent), dose based on body surface area:**<0.3 m<sup>2</sup>: 1 mg TID PRN nausea0.3–0.6 m<sup>2</sup>: 2 mg TID PRN nausea0.6–1 m<sup>2</sup>: 3 mg TID PRN nausea>1 m<sup>2</sup>: 4–8 mg TID PRN nausea**Dose based on age:**

&lt;4 yr: Use dose based on body surface area from preceding dosages.

4–11 yr: 4 mg TID PRN nausea

&gt;11 yr and adult: 8 mg TID or 24 mg once daily PRN nausea

**IV (child and adult):****Moderately emetogenic drugs:** 0.15 mg/kg/dose (**max. dose:** 8 mg/dose for child and 16 mg/dose adult) at 30 min before, 4 and 8 hr after emetogenic drugs. Then same dose Q4 hr PRN.*Continued*

ONDANSETRON *continued***IV (child and adult):**

**Highly emetogenic drugs:** 0.15 mg/kg/dose (**max. dose:** 16 mg/dose) 30 min before, 4 and 8 hr after emetogenic drugs. Then 0.15 mg/kg/dose (**max. dose:** 16 mg/dose) Q4 hr PRN.

**Preventing nausea and vomiting associated with surgery (additional doses for controlling nausea and vomiting may not provide any benefits):**

**IV/IM (administered before anesthesia over 2–5 min):****Child (2–12 yr):**

**≤40 kg:** 0.1 mg/kg/dose × 1

**>40 kg:** 4 mg × 1

**Adult:** 4 mg × 1

**PO:**

**Adult:** 16 mg × 1, 1 hr before induction of anesthesia

**Preventing nausea and vomiting associated with radiation therapy:**

**Child:** Use above dosage for preventing nausea and vomiting associated with chemotherapy, and give initial dose 1–2 hr before radiation.

**Adult:**

**Total body irradiation:** 8 mg PO 1–2 hr before radiation once daily

**Single high-dose fraction radiation to abdomen:** 8 mg PO 1–2 hr before radiation, with subsequent doses Q8 hr after first dose × 1–2 days after completion of radiation

**Daily fractionated radiation to abdomen:** 8 mg PO 1–2 hr before radiation, with subsequent doses Q8 hr after first dose for each day radiation is given

**Vomiting in acute gastroenteritis (PO route is preferred, use IV when PO is not possible):**

**PO (6 mo–10 yr and ≥8 kg; use oral disintegrating tablet):**

**8–15 kg:** 2 mg × 1

**>15 and ≤30 kg:** 4 mg × 1

**>30 kg:** 8 mg × 1

**IV (≥1 mo):** 0.15–0.3 mg/kg/dose × 1; **max. dose:** mg/dose

Avoid use in congenital long QTc syndrome. Bronchospasm, tachycardia, hypokalemia, seizures, headaches, lightheadedness, constipation, diarrhea, and transient increases in AST, ALT, and bilirubin may occur. Transient blindness (resolution within a few min up to 48 hr), arthralgia, hepatic dysfunction, and rare/transient ECG changes (including QTc interval prolongation) have been reported. Data limited for use in children <3 yr.

ECG monitoring is recommended in patients with electrolyte abnormalities, CHF, or bradyarrhythmias.

Drug clearance is higher for surgical and cancer patients <18 yr when compared with adults.

Clearance is slower for children 1–4 mo old compared with children >4–24 mo.

Ondansetron is a substrate for CYP 450 1A2, 2D6, 2E1, and 3A3/4 drug-metabolizing enzymes. It is likely that the inhibition/loss of one of the previously listed enzymes will be compensated by others and may result in insignificant changes to ondansetron's elimination. Ondansetron's elimination may be affected by CYP 450 enzyme inducers. Follow theophylline, phenytoin, or warfarin levels closely if used in combination. Use with apomorphine may result in profound hypotension and loss of consciousness and is **contraindicated**.



**OSETAMIVIR PHOSPHATE**

Tamiflu

**Antiviral**

No



Yes



2



C

**Caps:** 30, 45, 75 mg**Oral suspension:** 6 mg/mL (60 mL); may contain saccharin and sodium benzoate 

**NOTE:** Previous oral suspension concentration of 12 mg/mL has been replaced with a 6 mg/mL concentration so that both commercially available and compounded products are similar in concentration to prevent dosing errors.

**Treatment of influenza (initiate therapy within 2 days of onset of symptoms):**

**Preterm neonate (24–37 weeks' gestation; based on pharmacokinetic data from 20 neonates):** 1 mg/kg/dose PO BID

**Full-term neonate:**

**<14 days old:** 3 mg/kg/dose PO once daily × 5 days

**≥14 days old:** 3 mg/kg/dose PO BID × 5 days

**Child < 1 yr:** See following table



Age (months)	Dosage for 5 days	Volume of Oral Suspension (6 mg/mL)
<3	12 mg PO BID	2 mL
3–5	20 mg PO BID	3.33 mL
6–11	25 mg PO BID	4.2 mL

**Child ≥ 1–12 yr:** See following table.

Weight (kg)	Dosage for 5 days	Volume of Oral Suspension (6 mg/mL)
≤15	30 mg PO BID	5 mL
>15–23	45 mg PO BID	7.5 mL
>23–40	60 mg PO BID	10 mL
>40	75 mg PO BID	12.5 mL

**≥13 yr and adult:** 75 mg PO BID × 5 days

**Prophylaxis of influenza (initiate therapy within 2 days of exposure [see remarks]):**

**Child 3 mo–<1 yr:** 3 mg/kg/dose PO once daily

**Alternative dosage based on age:**

**3–5 mo:** 20 mg PO once daily

**6–11 mo:** 25 mg PO once daily

**Child 1–12 yr:**

**≤15 kg:** 30 mg PO once daily

**16–23 kg:** 45 mg PO once daily

**24–40 kg:** 60 mg PO once daily

**>40 kg:** 75 mg PO once daily

**≥13 yr and adult:** 75 mg PO once daily for a minimum of 7 days and up to 6 wk; initiate therapy within 2 days of exposure.

Currently indicated for treatment of influenza A and B strains. Use in children <1 yr has not been recommended owing to concerns of excessive CNS penetration and fatalities in 7-day-old rats.

Nausea and vomiting (generally occurring within first 2 days) are most common adverse effects.

Insomnia, vertigo, seizures, hypothermia, neuropsychiatric events (may result in fatal outcomes), arrhythmias, rash, and toxic epidermal necrolysis have also been reported. If GFR is 10–30 mL/min, reduce dosage to 75 mg PO once daily × 5 days for adults (see Chapter 31).

**PROPHYLAXIS USE:** Osetamivir is not a substitute for annual flu vaccination. Safety and efficacy have been demonstrated for ≤6 wk of therapy; duration of protection lasts for as long as dosing is continued. Adjust prophylaxis dose if GFR is 10–30 mL/min by extending dosage interval to once every other day.

*Continued*



OSELTAMIVIR PHOSPHATE *continued*

Probenecid increases oseltamivir levels. Oseltamivir decreases efficacy of the nasal influenza vaccine (FluMist; discontinue oseltamivir 48 hr before and **do not** restart for at least 1–2 wk after FluMist administration).

Dosage adjustments in hepatic impairment, severe renal disease, and dialysis have not been established for either treatment or prophylaxis use. Safety and efficacy of repeated treatment or prophylaxis courses have not been evaluated. Doses may be administered with or without food.

**OXACILLIN**

Various generic brands

**Antibiotic, penicillin (penicillinase resistant)**



Yes



Yes



2



B

**Injection:** 1, 2, 10 g

**Injection, premixed in iso-osmotic dextrose:** 1 g/50 mL, 2 g/50 mL

Injectable products contain 2.8–3.1 mEq Na per 1 g drug

**Neonate: IM/IV**

**≤7 days:**

**<1.2 kg:** 50 mg/kg/24 hr ÷ Q12 hr

**<1.2–2 kg:** 50–100 mg/kg/24 hr ÷ Q12 hr

**≥2 kg:** 75–150 mg/kg/24 hr ÷ Q8 hr

**>7 days:**

**<1.2 kg:** 50 mg/kg/24 hr ÷ Q12 hr

**1.2–2 kg:** 75–150 mg/kg/24 hr ÷ Q8 hr

**≥2 kg:** 100–200 mg/kg/24 hr ÷ Q6 hr

**Infant and child (IM/IV):** 100–200 mg/kg/24 hr ÷ Q4–6 hr (**max. dose:** 12 g/24 hr); use 200 mg/kg/24 hr for endocarditis and severe infections.

**Adult (IM/IV):** 250–2000 mg/dose Q4–6 hr; use higher dosage range for endocarditis or severe infections. **Max. dose:** 12 g/24 hr.

Rash and GI disturbances are common. Leukopenia, reversible hepatotoxicity, and acute interstitial nephritis has been reported. Hematuria and azotemia have occurred in neonates and infants with high doses. May cause false-positive urinary and serum proteins.

Probenecid increases serum oxacillin levels. Tetracyclines may antagonize the bactericidal effects of oxacillin.

CSF penetration is poor unless meninges are inflamed. Use the lower end of the usual dosage range for patients with creatinine clearances <10 mL/min. **Adjust dose in renal failure (see Chapter 31).**

**OXCARBAZEPINE**

Trileptal, Oxtellar, and generics

**Anticonvulsant**



No



Yes



2



C

**Tabs:** 150, 300, 600 mg

**Extended-release tabs (Oxtellar):** 150, 300, 600 mg

**Oral suspension:** 300 mg/5 mL (250 mL); contains saccharin, ethanol, and propylene glycol

**IMMEDIATE-RELEASE PRODUCT:**

**Child (2–<4 yr):**

**Adjunctive therapy:** Start with 8–10 mg/kg/24 hr PO ÷ BID up to a **max. dose** of 600 mg/24 hr.

For children <20 kg, may consider using a starting dose of 16–20 mg/kg/24 hr PO ÷ BID;

gradually increase the dose over a 2–4-week period and **do not exceed** 60 mg/kg/24 hr ÷ BID.

OXCARBAZEPINE *continued***IMMEDIATE-RELEASE PRODUCT:****Child (4–16 yr [see remarks]):**

**Adjunctive therapy:** Start with 8–10 mg/kg/24 hr PO ÷ BID up to a **max. dose** of 600 mg/24 hr. Then gradually increase dose over a 2-wk period to the following maintenance doses:

**20–29 kg:** 900 mg/24 hr PO ÷ BID

**29.1–39 kg:** 1200 mg/24 hr PO ÷ BID

**>39 kg:** 1800 mg/24 hr PO ÷ BID

**Conversion to monotherapy:** Start with 8–10 mg/kg/24 hr PO ÷ BID, and simultaneously initiate dosage reduction of concomitant AEDs and withdraw completely over 3–6 wk. Dose may be increased at weekly intervals (as clinically indicated) by a **max.** of 10 mg/kg/24 hr to achieve recommended monotherapy maintenance dose as described in the following table.

**Initiation of monotherapy:** Start with 8–10 mg/kg/24 hr PO ÷ BID. Then increase by 5 mg/kg/24 hr Q3 days up to recommended monotherapy maintenance dose as described in the following table:

Recommended Monotherapy Maintenance Doses for Children by Weight

Weight (kg)	Daily Oral Maintenance Dose (mg/24 hr) Divided BID
20–<25	600–900
25–<35	900–1200
35–<45	900–1500
45–<50	1200–1500
50–<60	1200–1800
60–<70	1200–2100
≥70	1500–2100

**Adult:**

**Adjunctive therapy:** Start with 600 mg/24 hr PO ÷ BID. Dose may be increased at weekly intervals (as clinically indicated) by a **max.** of 600 mg/24 hr. Usual maintenance dose is 1200 mg/24 hr PO ÷ BID. Doses ≥2400 mg/24 hr are generally not well tolerated owing to CNS side effects.

**Conversion to monotherapy:** Start with 600 mg/24 hr PO ÷ BID, and simultaneously initiate dosage reduction of concomitant AEDs. Dose may be increased at weekly intervals (as clinically indicated) by a **max.** of 600 mg/24 hr to achieve a dose of 2400 mg/24 hr PO ÷ BID. Concomitant AEDs should be terminated gradually over ≈ 3–6 wk.

**Initiation of monotherapy:** Start with 600 mg/24 hr PO ÷ BID. Then increase by 300 mg/24 hr Q3 days up to 1200 mg/24 hr PO ÷ BID.

**EXTENDED-RELEASE TABS (Oxtellar [see remarks]):****Child 6–17 yr:**

**Adjunctive therapy:** Start with 8–10 mg/kg/24 hr PO once daily up to a **max. dose** of 600 mg/24 hr. Then gradually increase at weekly intervals in 8–10 mg/kg/24 hr increments (**max. dosage increment:** 600 mg) to the following maintenance doses:

**20–29 kg:** 900 mg PO once daily

**29.1–39 kg:** 1200 mg PO once daily

**≥39.1 kg:** 1800 mg PO once daily

**Adult:**

**Adjunctive therapy:** Start with 600 mg PO once daily (consider using 900 mg if receiving concomitant enzyme-inducing antiepileptic drugs). Then gradually increase at weekly intervals in 600 mg/24 hr increments to the maintenance dose of 1200–2400 mg once daily.

**Clinically significant hyponatremia may occur; generally seen within first 3 mo of therapy.**

May also cause headache, dizziness, drowsiness, ataxia, fatigue, nystagmus, urticaria, diplopia, abnormal gait, and GI discomfort. About 25% to 30% of patients with carbamazepine hypersensitivity will experience a cross-reaction with oxcarbazepine. Serious

*Continued*



OXCARBAZEPINE *continued*

dermatologic reactions (Stevens-Johnson syndrome and TEN), multiorgan hypersensitivity reactions, bone marrow depression, pancreatitis, folic acid deficiency, hypothyroidism, rare cases of anaphylaxis and angioedema, and suicidal behavior or ideation have been reported.

Inhibits CYP 450 2C19 and induces CYP 450 3A4/5 drug-metabolizing enzymes. Carbamazepine, cyclosporine, phenobarbital, phenytoin, valproic acid, and verapamil may decrease oxcarbazepine levels. Oxcarbazepine may increase phenobarbital and phenytoin levels. Oxcarbazepine can decrease effects of oral contraceptives, felodipine, and lamotrigine.

If GFR < 30 mL/min, adjust dosage by administering 50% of normal starting dose (**max. dose:** 300 mg/24 hr), followed by a slower-than-normal increase in dose if necessary (**see Chapter 31**). No dosage adjustment required in mild/moderate hepatic impairment. Use is **not recommended** in severe hepatic impairment owing to lack of information.

Extended-release and immediate-release products are not bioequivalent; higher doses of the extended-release product may be necessary. Doses may be administered with or without food.

**OXYBUTYNIN CHLORIDE**

Ditropan, Ditropan XL, Oxytrol, and generics

**Anticholinergic agent, antispasmodic**



Yes



Yes



2



B

**Tab:** 5 mg

**Tab, extended-release (Ditropan XL and generics):** 5, 10, 15 mg

**Syrup:** 1 mg/mL (473 mL); contains parabens

**Transdermal system (Oxytrol):** Delivers 3.9 mg/24 hr (1, 2s, 4s, 8s); contains 36 mg per system

**Child ≤ 5 yr:**

**Immediate release:** 0.2 mg/kg/dose BID–TID PO; **max. dose:** 15 mg/24 hr

**Child > 5 yr:**

**Immediate release:** 5 mg/dose BID–TID PO; **max. dose:** 15 mg/24 hr

**Extended release (≥ 6 yr):** Start with 5 mg/dose once daily PO; if needed, increase as tolerated by 5-mg increments up to a **max.** of 20 mg/24 hr.

**Adult:**

**Immediate release:** 5 mg/dose BID–TID PO

**Extended release (Ditropan XL):** 5–10 mg/dose once daily PO up to a **max. dose** of 30 mg/dose once daily PO

**Transdermal system:** 1 patch (3.9 mg/24 hr) Q3–4 days (twice weekly)

**Use with caution** in hepatic or renal disease, hyperthyroidism, IBD, or cardiovascular disease.

Anticholinergic side effects may occur, including drowsiness and hallucinations.

**Contraindicated** in glaucoma, GI obstruction, megacolon, myasthenia gravis, severe colitis, hypovolemia, and GU obstruction. Memory impairment, angioedema, and QT interval prolongation have been reported. Oxybutynin is a CYP 450 3A4 substrate; inhibitors and inducers of CYP 450 3A4 may increase and decrease effects of oxybutynin, respectively.

Dosage adjustments for extended-release dosage form are at weekly intervals. **Do not** crush, chew, or divide extended-release tablets. Apply transdermal system on dry intact skin on the abdomen, hip, or buttock by rotating the site and avoiding same site application within 7 days.



**OXYCODONE**

OxyContin, Roxicodone, and many others

**Narcotic, analgesic**

Yes



Yes



2



B/D

**Solution:** 1 mg/mL (5, 15, 500 mL); contains alcohol**Concentrated solution:** 20 mg/mL (30 mL); may contain saccharin**Tabs:** 5, 10, 15, 20, 30 mg**Controlled-release tabs (OxyContin and others):** 10, 15, 20, 30, 40, 60, 80 mg (80-mg strength for opioid-tolerant patients only)**Caps:** 5 mg**Opioid-naïve doses based on oxycodone salt:****Child:** 0.05–0.15 mg/kg/dose Q4–6 hr PRN up to 5 mg/dose PO**Adolescent (≥50 kg) and adult:** 5–10 mg Q4–6 hr PRN PO; see remarks for use of controlled-release tablets.

Abuse potential, CNS and respiratory depression, increased ICP, histamine release, constipation, and GI distress may occur. **Use with caution** in severe renal impairment (increases  $T_{1/2}$ ) and mild/moderate hepatic dysfunction (use  $\frac{1}{3}$  to  $\frac{1}{2}$  of usual dose has been recommended). **Naloxone is the antidote.** See Chapter 6 for equianalgesic dosing. Check dosages of acetaminophen or aspirin when using combination products (e.g., Tylox, Percodan). Aspirin is **not recommended** in children due to concerns of Reye syndrome. Oxycodone is metabolized by the CYP 450 3A4 (major) and 2D6 (minor) isoenzyme.



When using controlled-release tablets (OxyContin), determine patient's total 24-hr requirements and divide by 2 to administer on a Q12-hr dosing interval. OxyContin 80-mg tablet is **USED ONLY** for opioid-tolerant patients; this strength can cause fatal respiratory depression in opioid-naïve patients. Controlled-release dosage form **should not be used** as a PRN analgesic and must be swallowed whole.

Pregnancy category changes to "D" if used for prolonged periods or in high doses at term.

**OXYCODONE AND ACETAMINOPHEN**

Endocet, Roxilox, Percocet, Roxicet, Roxicet 5/500, and many others

**Combination analgesic with narcotic**

Yes



Yes



2



C

**Capsule or caplet (Roxilox 5/500):** oxycodone HCl 5 mg + acetaminophen 500 mg**Tabs (Percocet, Endocet, and others):****Most common strength:** Oxycodone HCl 5 mg + acetaminophen 325 mg**Other strengths:**

Oxycodone HCl 2.5 mg + acetaminophen 325 mg

Oxycodone HCl 7.5 mg + acetaminophen 325 mg or 500 mg

Oxycodone HCl 10 mg + acetaminophen 325 mg or 650 mg

**Oral solution (Roxicet):** Oxycodone HCl 5 mg + acetaminophen 325 mg/5 mL (5, 500 mL); contains 0.4% alcohol and saccharin

Dose based on amount of oxycodone and acetaminophen. Do not exceed 4 g/24 hr of acetaminophen.



See *Oxycodone* and *Acetaminophen*. Check dosages of acetaminophen when using these combination products.



**OXYCODONE AND ASPIRIN**

Percodan, Endodan, and generics

**Combination analgesic (narcotic and salicylate)**

Yes



Yes



2



D

**Tabs:** Oxycodone 4.8355 mg and aspirin 325 mg

Dose based on amount of oxycodone and aspirin. Do not exceed 4 g/24 hr of aspirin.

See *Oxycodone* and *Aspirin*. **Do not use** in children <16 yr because of risk for Reye syndrome.

Check dosages of aspirin when using these combination products.

**OXYMETAZOLINE****Nasal:** Afrin 12 Hour, Duramist 12-Hr Nasal, Neo-Synephrine 12-Hour Nasal, Nostrilla, and many others**Ophthalmic:** Visine LR**Nasal decongestant, vasoconstrictor**

No



No



?



C

**Nasal spray [OTC]:** 0.05% (15, 30 mL); may contain benzalkonium chloride and propylene glycol**Ophthalmic drops [OTC]:** 0.025% (15 mL); contains benzalkonium chloride and EDTA**Nasal decongestant (not to exceed 3 days in duration):**

≥6 yr—adult: 2–3 sprays or 2–3 drops or 1–2 metered sprays (Nostrilla) in each nostril BID.

**Do not exceed** 2 doses/24 hr period.**Ophthalmic:**

≥6 yr—adult: Instill 1–2 drops in affected eye(s) Q6 hr.

**Contraindicated** in patients on MAO inhibitor therapy. Rebound nasal congestion may occur with excessive use (>3 days) via nasal route. Systemic absorption may occur with either route of administration. Headache, dizziness, hypertension, transient burning, stinging, dryness, nasal mucosa ulceration, sneezing, blurred vision, and mydriasis have occurred.**Do not use** ophthalmic solution if it changes color or becomes cloudy.

Accidental ingestion of either dosage form in children &lt;5 yr has been reported and required hospitalization for adverse events (nausea, vomiting, lethargy, tachycardia, respiratory depression, bradycardia, hypotension, hypertension, sedation, mydriasis, stupor, hypothermia, drooling, and coma).

**PALIVIZUMAB**

Synagis

**Monoclonal antibody**

No



No



?



C

**Injection, solution:** 100 mg/mL (0.5, 1 mL; single use); contains glycine and histidine**RSV prophylaxis during RSV season for the following age and clinical criteria (see latest edition of AAP Red Book for most recent indications):**

&lt;3 mo of age, born at 32–&lt;35 wk' gestation, and with either daycare attendance or &gt;1 sibling (&lt;5 yr old) living in the same household

&lt;6 mo of age and born at 29–&lt;32 wk' gestation

&lt;12 mo of age and one of the following:

Born at ≤28 wk' gestation; OR



PALIVIZUMAB *continued*

With congenital airway abnormalities or neuromuscular disorders that decrease ability to manage airway secretions

≤24 mo of age and one of the following:

With chronic lung disease requiring medical therapy within 6 mo before start of RSV season; OR

With congenital heart disease and one of the following conditions: Cyanotic heart, moderate/severe pulmonary hypertension, or receiving CHF pharmacotherapy

**DOSE:** 15 mg/kg/dose IM Q monthly just before and during RSV season

RSV season typically November through April in Northern Hemisphere but may begin earlier or persist later in certain communities. IM is currently the only route of administration, so **use with caution** in patients with thrombocytopenia or any coagulation disorder. The following adverse effects have been reported at slightly higher incidences when compared with placebo: rhinitis, rash, pain, increased liver enzymes, pharyngitis, cough, wheeze, diarrhea, vomiting, conjunctivitis, and anemia. Rare acute hypersensitivity reactions have been reported (first or subsequent doses).

Does not interfere with response to routine childhood vaccines. May interfere with immunologic-based RSV diagnostic tests (some antigen detection–based assays and viral culture assays), but not with reverse transcriptase–PCR-based assays.

Palivizumab is currently indicated for RSV prophylaxis in high-risk infants only. Efficacy and safety have not been demonstrated for treatment of RSV.

Each dose should be administered IM in anterolateral aspect of thigh. It is recommended to divide doses with total injection volumes >1 mL. **Avoid** injection in gluteal muscle because of risk for damage to sciatic nerve.

**PANCREATIC ENZYMES**

See Chapter 30 for description and contents of lipase, protease, and amylase.



No



No



2



C

**Initial doses (actual requirements are patient specific):**

**Enteric-coated microspheres and microtabs:**

**Infant:** 2000–4000 U lipase per 120 mL (formula or breast milk)

**Child < 4 yr:** 1000 U lipase/kg/meal

**Child ≥ 4 yr and adult:** 500 U lipase/kg/meal

**Max. dose** (child–adult): 2500 U lipase/kg/meal, or 10,000 U lipase/kg/24 hr, or 4000 U lipase/g fat/24 hr

Total daily dose should include ≈ 3 meals and 2–3 snacks per day. Snack doses are ≈ half of meal doses, depending on amount of fat and food consumed.

May cause occult GI bleeding, allergic reactions to porcine proteins, hyperuricemia, and hyperuricosuria with high doses. Dose should be titrated to eliminate diarrhea and minimize steatorrhea. **Do not** chew microspheres or microtabs. Concurrent administration with H<sub>2</sub> antagonists or gastric acid pump inhibitors may enhance enzyme efficacy. Doses higher than 6000 U lipase/kg/meal have been associated with colonic strictures in children <12 yr. Powder dosage form is **not** preferred, owing to potential GI mucosal ulceration.

**Avoid use** of generic pancreatic enzyme products because they have been associated with treatment failures. Products not approved by the FDA are no longer allowed to be distributed in the United States.

**PANCURONIUM BROMIDE**

Various generic brands

**Nondepolarizing neuromuscular blocking agent**

Yes



Yes



?



C

**Injection:** 1 mg/mL (10 mL), 2 mg/mL (2, 5 mL); contains benzyl alcohol**Intermittent dosing (see remarks):****Neonate:****Initial:** 0.02 mg/kg/dose IV**Maintenance:** 0.05–0.1 mg/kg/dose IV Q0.5–4 hr PRN**1 mo–adult:****Initial:** 0.04–0.1 mg/kg/dose IV**Maintenance:** 0.015–0.1 mg/kg/dose IV Q30–60 min**Continuous IV infusion (see remarks):****Neonate:** 0.02–0.04 mg/kg/hr**Child:** 0.03–1 mg/kg/hr**Adolescent and adult:** 0.02–0.04 mg/kg/hr

Onset of action is 1–2 min. May cause tachycardia, salivation, and wheezing. Severe anaphylactic reactions have been reported; cross-reactivity between neuromuscular blocking agents has been reported.

Drug effects may be accentuated by hypothermia, acidosis, neonatal age, decreased renal function, halothane, succinylcholine, hypokalemia, hyponatremia, hypocalcemia, clindamycin, tetracycline, and aminoglycoside antibiotics. Drug effects may be antagonized by alkalosis, hypercalcemia, peripheral neuropathies, diabetes mellitus, demyelinating lesions, carbamazepine, phenytoin, theophylline, anticholinesterases (e.g., neostigmine, pyridostigmine), and azathioprine. For obese patients, use of lean body weight for dose calculation has been recommended to prevent intense block of long duration and possible overdose.

**Antidote is neostigmine** (with atropine or glycopyrrolate). **Avoid** use in severe renal impairment (<10 mL/min). Patients with cirrhosis may require a high initial dose to achieve adequate relaxation, but muscle paralysis will be prolonged.

**PANTOPRAZOLE**

Protonix and generics

**Gastric acid pump inhibitor**

Yes



No



2



B

**Tab, delayed release, enteric coated:** 20, 40 mg**Injection:** 40 mg; contains edetate sodium**Oral suspension:** 2 mg/mL; contains 0.25 mEq sodium bicarbonate per 1 mg drug**Powder for delayed-release oral suspension (Protonix):** 40 mg (30s); contains polysorbate 80**Child (see remarks):****GERD (limited data):**

**Infant and < 5 yr:** 1.2 mg/kg/24 hr PO once daily. **Note:** Pantoprazole did not significantly improve GERD symptom scores in an open-label trial in 128 infants (1–11 mo) receiving 1.2 mg/kg/24 hr PO once daily  $\times$  4 wk, followed by a 4-wk double-blinded placebo-controlled withdrawal phase.

**$\geq 5$  yr and adolescent:** 20 or 40 mg PO once daily

**GERD with erosive esophagitis:**

**1–5 yr (limited data):** 0.3, 0.6, or 1.2 mg/kg/24 hr PO once daily all improved GERD symptoms in an 8-wk multicenter randomized placebo-controlled trial for 60 subjects with GERD and histologic/erosive esophagitis.

PANTOPRAZOLE *continued***GERD with erosive esophagitis:****≥5 yr (up to 8 wk of therapy):****15–<40 kg:** 20 mg PO once daily**≥40 kg:** 40 mg PO once daily

**IV (data limited to pharmacokinetic trials):** Some doses ranging from 0.32–1.88 mg/kg/dose have been reported from three separate trials (total N = 31; 0.01–16.4 yr). Patients with systemic inflammatory response syndrome (SIRS) cleared the drug more slowly, resulting in higher  $T_{1/2}$  and AUC, than patients without. Despite limited data, doses of 1–2 mg/kg/24 hr ÷ Q12–24 hr have been used. Additional studies are needed.

**Adult:**

**GERD with erosive esophagitis:** 40 mg PO once daily × 8–16 wk or 40 mg IV once daily × 7–10 days

**Peptic ulcer:** 40–80 mg PO once daily × 4–8 wk

**Hypersecretory conditions:**

**PO:** 40 mg BID; dose may be increased as needed up to a **max. dose** of 240 mg/24 hr.

**IV:** 80 mg Q12 hr; dose may be increased as needed to Q8 hr (**max. dose:** 240 mg/24 hr). Therapy > 6 days at 240 mg/24 hr has not been evaluated.

Convert from IV to PO therapy as soon as patient is able to tolerate PO. Common side effects include diarrhea and headache. May cause transient elevation in LFTs. Like other PPIs, may increase risk for *C. difficile*-associated diarrhea. Hypomagnesemia has been reported with long-term use. Drug is a substrate for CYP 450 2C19 (major), 2D6 (minor), and 3A3/4 (minor) isoenzymes. May decrease absorption of itraconazole, ketoconazole, iron salts, and ampicillin esters. May increase effect/toxicity of methotrexate.



Children 1–2 yr of age have demonstrated more rapid clearance of pantoprazole in pharmacokinetic studies; this age group may require higher doses. All oral doses may be taken with or without food.

**Do not** crush or chew tablets. Extemporaneously compounded oral suspension may be less bioavailable owing to loss of enteric coating. Powder for delayed-release oral suspension product may be mixed with 5 mL apple juice (administer immediately, followed by rinsing container with more apple juice) or sprinkled on 1 teaspoonful of applesauce (administer within 10 min); see package insert for NG administration.

For IV infusion, doses may be administered over 15 min at a concentration of 0.4–0.8 mg/mL or over 2 min at a concentration of 4 mg/mL. Midazolam and zinc are **not compatible** with the IV dosage form. Parenteral routes other than IV are **not recommended**.

**PAROMOMYCIN SULFATE**

Humatin and generics

**Amebicide, antibiotic (aminoglycoside)**

No



No



1



?

**Caps:** 250 mg

**Intestinal amebiasis** (*Entamoeba histolytica*), *Dientamoeba fragilis*, and *Giardia lamblia* infection:

**Child and adult:** 25–35 mg/kg/24 hr PO ÷ Q8 hr × 7 days

**Tapeworm** (*Taenia saginata*, *Taenia solium*, *Diphyllobothrium latum*, and *Dipylidium caninum*):

**Child:** 11 mg/kg/dose PO Q15 min × 4 doses

**Adult:** 1 g PO Q15 min × 4 doses

**Tapeworm** (*Hymenolepis nana*):

**Child and adult:** 45 mg/kg/dose PO once daily × 5–7 days

*Continued*

PAROMOMYCIN SULFATE *continued***Cryptosporidial diarrhea:**

**Adult:** 1.5–2.25 g/24 hr PO ÷ 3–6 × daily. Duration varies from 10–14 days to 4–8 wk. Maintenance therapy has also been used. Alternatively, 1 g PO BID × 12 wk in conjunction with azithromycin 600 mg PO once daily × 4 wk has been used in patients with AIDS.

**Contraindicated** in intestinal obstruction. **Use with caution** in ulcerative bowel lesions to avoid renal toxicity via systemic absorption. Drug is generally poorly absorbed and therefore **not** indicated for sole treatment of extraintestinal amebiasis. Side effects include GI disturbance, hematuria, rash, ototoxicity, and hypocholesterolemia. Bacterial overgrowth of nonsusceptible organisms, including fungi, may occur. May decrease effects of digoxin.

Pregnancy category has not been formally assigned by the FDA.

**PAROXETINE**

Paxil, Pexeva, Paxil CR, Brisdelle, and generics

**Antidepressant, selective serotonin reuptake inhibitor**



Yes



Yes



2



X

**Tabs:** 10, 20, 30, 40 mg

**Caps (Brisdelle):** 7.5 mg

**Controlled-release tabs (Paxil CR and generics):** 12.5, 25, 37.5 mg

**Oral suspension:** 10 mg/5 mL (250 mL); contains saccharin and parabens

**Child:**

**Depression:** Well-controlled clinical trials have failed to demonstrate efficacy in children.

The FDA recommends paroxetine not be used for this indication.

**Obsessive-compulsive disorder (limited data, based on a 10-wk randomized controlled trial in 207 children 7–17 yr; mean age 11.1 ± 3.03 yr):** Start with 10 mg PO once daily. If needed, adjust upwards by increasing dose no more than 10 mg/24 hr, no more frequently than Q7 days, up to a **max. dose** of 50 mg/24 hr. Mean doses of 20.3 mg/24 hr (children) and 26.8 mg/24 hr (adolescents) were used.

**Social anxiety disorder (8–17 yr):** Start with 10 mg PO once daily. If needed, increase dose by 10 mg/24 hr no more frequently than Q7 days up to a **max. dose** of 50 mg/24 hr.

**Adult:**

**Depression:** Start with 20 mg PO QAM × 4 wk. If no clinical improvement, increase dose by 10 mg/24 hr Q7 days PRN up to a **max. dose** of 50 mg/24 hr.

**Paxil CR:** Start with 25 mg PO QAM × 4 wk. If no improvement, increase dose by 12.5 mg/24 hr Q7 days PRN up to a **max. dose** of 62.5 mg/24 hr.

**Obsessive compulsive disorder:** Start with 20 mg PO once daily; increase dose by 10 mg/24 hr Q7 days PRN up to a **max. dose** of 60 mg/24 hr. Usual dose is 40 mg PO once daily.

**Panic disorder:** Start with 10 mg PO QAM; increase dose by 10 mg/24 hr Q7 days PRN up to a **max. dose** of 60 mg/24 hr.

**Paxil CR:** Start with 12.5 mg PO QAM; increase dose by 12.5 mg/24 hr Q7 days PRN up to a **max. dose** of 75 mg/24 hr.

**Contraindicated** in patients taking MAOIs (within 14 days of discontinuing MAOIs), pimozide, or thioridazine. **Use with caution** in patients with history of seizures, renal or hepatic impairment, cardiac disease, suicidal concerns, mania/hypomania, and diuretic use. Patients with severe renal or hepatic impairment should initiate therapy at 10 mg/24 hr and increase dose as needed up to a **max. dose** of 40 mg/24 hr.

Common side effects include anxiety, nausea, anorexia, and decreased appetite. Monitor for clinical worsening of depression and suicidal ideation/behavior after initiation of therapy or after dose changes. Stevens-Johnson syndrome has been reported.



PAROXETINE *continued*

Paroxetine is an inhibitor and substrate for CYP 450 2D6. May increase effects/toxicity of tricyclic antidepressants, theophylline, and warfarin. May decrease effects of tamoxifen. Cimetidine, ritonavir, MAOIs (fatal serotonin syndrome), dextromethorphan, phenothiazines, and type 1C antiarrhythmics may increase effect/toxicity of paroxetine. Weakness, hyperreflexia, and poor coordination have been reported when taken with sumatriptan.

**Do not discontinue therapy abruptly;** may cause sweating, dizziness, confusion, and tremor. May be taken with or without food.

**PENICILLIN G PREPARATIONS—AQUEOUS POTASSIUM AND SODIUM**

Pfizerpen and others

**Antibiotic, aqueous penicillin**

No



Yes



2



B

**Injection (K<sup>+</sup>):** 5, 20 million units (contains 1.7 mEq K and 0.3 mEq Na/1 million units penicillin G)

**Premixed frozen injection (K<sup>+</sup>):** 1 million units in 50 mL dextrose 4%; 2 million units in 50 mL dextrose 2.3%; 3 million units in 50 mL dextrose 0.7% (contains 1.7 mEq K and 0.3 mEq Na/1 million units penicillin G)

**Injection (Na<sup>+</sup>):** 5 million units (contains 2 mEq Na/1 million units penicillin G)

Conversion: 250 mg = 400,000 units

**Neonate (IM/IV; use higher end of dosage range for meningitis and severe infections):**

**≤ 7 days:**

≤ 2 kg: 50,000–100,000 units/kg/24 hr ÷ Q12 hr

> 2 kg: 75,000–150,000 units/kg/24 hr ÷ Q8 hr

**> 7 days:**

< 1.2 kg: 50,000–100,000 units/kg/24 hr ÷ Q12 hr

1.2–2 kg: 75,000–150,000 units/kg/24 hr ÷ Q8 hr

≥ 2 kg: 100,000–200,000 units/kg/24 hr ÷ Q6 hr

**Group B streptococcal meningitis:**

≤ 7 days: 250,000–450,000 units/kg/24 hr ÷ Q8 hr

> 7 days: 450,000–500,000 units/kg/24 hr ÷ Q4–6 hr

**Congenital syphilis (total of 10 days of therapy; if > 1 day of therapy is missed, restart the entire course):**

≤ 7 days: 100,000 units/kg/24 hr ÷ Q12 hr IV; increase to dosage below at day 8 of life

> 7 days: 150,000 units/kg/24 hr ÷ Q8 hr IV

**Infant and child:**

**IM/IV (use higher end of dosage range and Q4 hr interval for meningitis and severe infections):**

100,000–400,000 units/kg/24 hr ÷ Q4–6 hr; **max. dose:** 24 million units/24 hr

**Neurosyphilis:** 200,000–300,000 units/kg/24 hr ÷ Q4–6 hr IV × 10–14 days; **max. dose:** 24 million units/24 hr

**Adult:**

**IM/IV:** 4–24 million units/24 hr ÷ Q4–6 hr

**Neurosyphilis:** 18–24 million units/24 hr ÷ Q4–6 hr IV × 10–14 days

Use penicillin V potassium for oral use. Side effects: anaphylaxis, urticaria, hemolytic anemia, interstitial nephritis, Jarisch-Herxheimer reaction (syphilis). Preparations containing potassium and/or sodium salts may alter serum electrolytes.  $T_{1/2}$  = 30 min; may be prolonged by concurrent use of probenecid. For meningitis, use higher daily dose at shorter dosing intervals. For treatment of anthrax (*Bacillus anthracis*), see [www.bt.cdc.gov](http://www.bt.cdc.gov) for additional information. **Adjust dose in renal impairment (see Chapter 31).**

Tetracyclines, chloramphenicol, and erythromycin may antagonize penicillin's activity. Probenecid increases penicillin levels. May cause false-positive or -negative urinary glucose (Clinistest method), false-positive direct Coombs test, and false-positive urinary and/or serum proteins.





**PENICILLIN G PREPARATIONS—BENZATHINE**

Bicillin L-A

**Antibiotic, penicillin (very long-acting IM)**

No



Yes



2



B

**Injection:** 600,000 units/mL (1, 2, 4 mL); contains parabens and povidone**Injection should be IM only.****Group A streptococci:****Infant and child:** 25,000–50,000 units/kg/dose IM  $\times$  1; **max. dose:** 1.2 million units/dose**OR:****>1 mo and <27 kg:** 600,000 units/dose IM  $\times$  1 **$\geq$ 27 kg and adult:** 1.2 million units/dose IM  $\times$  1**Rheumatic fever prophylaxis (Q3 wk administration recommended for high-risk situations):****Infant and child (>1 mo and <27 kg):** 600,000 units/dose IM Q3–4 wk**Adult:** 1.2 million units/dose IM Q3–4 wk**Syphilis (if >1 day of therapy is missed, restart the entire course; divided total dose into two injection sites):****Infant and child:****Primary, secondary, and early latent syphilis (<1 yr duration):** 50,000 units/kg/dose  $\times$  1**Late latent syphilis or latent syphilis of unknown duration:** 50,000 units/kg/dose Q7 days  $\times$  3 doses**Max. dose:** 2.4 million units/dose**Adult:****Primary, secondary, and early latent syphilis:** 2.4 million units/dose IM  $\times$  1**Late latent syphilis or latent syphilis of unknown duration:** 2.4 million units/dose IM Q7 days  $\times$  3 dosesProvides sustained levels for 2–4 wk. **Use with caution** in renal failure, asthma, and cephalosporin hypersensitivity. Side effects and drug interactions same as for *Penicillin G Preparations—Aqueous Potassium and Sodium*. Injection site reactions are common.**Deep IM administration only. Do not administer IV** (cardiac arrest and death may occur) and **do not inject** into or near an artery or nerve (may result in permanent neurologic damage).**PENICILLIN G PREPARATIONS—PENICILLIN G BENZATHINE AND PENICILLIN G PROCAINE**

Bicillin C-R, Bicillin C-R 900/300

**Antibiotic, penicillin (very long-acting IM)**

No



Yes



2



B

**Bicillin CR:** 300,000 units penicillin G procaine + 300,000 units penicillin G benzathine/mL to provide 600,000 units penicillin per 1 mL (2-mL Tubex syringe)**Bicillin CR (900/300):** 150,000 units penicillin G procaine + 450,000 units penicillin G benzathine/mL (2-mL Tubex syringe)

All preparations contain parabens and povidone.

**Injection should be for IM use only.****Dosage based on total amount of penicillin.****Group A streptococci:****Child < 14 kg:** 600,000 units/dose IM  $\times$  1**Child 14–27 kg:** 900,000–1,200,000 units/dose IM  $\times$  1**Child > 27 kg and adult:** 2,400,000 units/dose IM  $\times$  1

# PENICILLIN G PREPARATIONS—PENICILLIN G BENZATHINE AND PENICILLIN G PROCAINE *continued*

This preparation provides early peak levels in addition to prolonged levels of penicillin in the blood. **Do not use this product to treat syphilis; treatment failure can occur. Use with caution** in renal failure, asthma, significant allergies, and cephalosporin hypersensitivity. Addition of procaine penicillin has not been shown more efficacious than benzathine alone, but it may reduce injection discomfort.

**Deep IM administration only. Do not administer IV** (cardiac arrest and death may occur), and **do not inject** into or near an artery or nerve (may result in permanent neurologic damage).

Side effects and drug interactions same as for *Penicillin G Preparations—Aqueous Potassium and Sodium*. Immune hypersensitivity reaction has been reported.

## PENICILLIN G PREPARATIONS—PROCAINE

Wycillin and generics

**Antibiotic, penicillin (long-acting IM)**



No



Yes



2



B

**Injection:** 600,000 units/mL (1, 2 mL); may contain parabens, phenol, povidone, and formaldehyde  
Contains 120 mg procaine per 300,000 units penicillin

**Injection should be for IM use only.**

**Newborn (see remarks):** 50,000 units/kg/24 hr IM once daily

**Infant and child:** 25,000–50,000 units/kg/24 hr ÷ Q12–24 hr IM; **max. dose:** 4.8 million units/24 hr

**Adult:** 0.6–4.8 million units/24 hr ÷ Q12–24 hr IM

**Congenital syphilis, syphilis (if >1 day of therapy is missed, restart the entire course):**

**Neonate, infant, child:** 50,000 units/kg/dose once daily IM × 10 days

**Neurosyphilis:**

**Adult:** 2.4 million units IM once daily and Probenecid 500 mg Q6 hr PO × 10–14 days (both medications)

**Inhaled anthrax:** Postexposure prophylaxis (total duration of therapy with all forms of therapy is 60 days; switch to alternative form of therapy after 2 wk of procaine penicillin because of risk for adverse effects):

**Child:** 25,000 units/kg/dose (**max. dose:** 1.2 million units/dose) IM Q12 hr

**Adult:** 1.2 million units IM Q12 hr

Provides sustained levels for 2–4 days. **Use with caution** in renal failure, asthma, significant allergies, cephalosporin hypersensitivity, and in neonates (higher incidence of sterile abscess at injection site and risk of procaine toxicity). Side effects and drug interactions similar to *Penicillin G Preparations—Aqueous Potassium and Sodium*. In addition, may cause CNS stimulation and seizures. Immune hypersensitivity reaction has been reported.

**Deep IM administration only. Do not administer IV** (cardiac arrest and death may occur) and **do not inject** into or near an artery or nerve (may result in permanent neurologic damage). Large doses may be administered in two injection sites. No longer recommended for empirical treatment of gonorrhea due to resistant strains.

**PENICILLIN V POTASSIUM**

Veetids and generics

**Antibiotic, penicillin**

No



Yes



2



B

**Tabs:** 250, 500 mg**Oral solution:** 125 mg/5 mL, 250 mg/5 mL (100, 200 mL); may contain saccharin

Contains 0.7 mEq potassium/250 mg drug

250 mg = 400,000 units

**Child:** 25–50 mg/kg/24 hr ÷ Q6–8 hr PO; **max. dose:** 3 g/24 hr**Adolescent and adult:** 125–500 mg/dose PO Q6–8 hr**Acute group A streptococcal pharyngitis (use BID dosing regimen ONLY if good compliance is expected):****Child < 27 kg:** 250 mg PO BID–TID × 10 days**≥27 kg, adolescent and adult:** 500 mg PO BID–TID × 10 days**Rheumatic fever prophylaxis and pneumococcal prophylaxis for sickle cell disease and functional or anatomic asplenia (regardless of immunization status):****2 mo–<3 yr:** 125 mg PO BID**3–5 yr:** 250 mg PO BID. For sickle cell and asplenia, use may be discontinued after age 5 if child received recommended pneumococcal immunizations and did not experience invasive pneumococcal infection.**Recurrent rheumatic fever prophylaxis:****Child and adult:** 250 mg PO BIDSee *Penicillin G Preparations—Aqueous Potassium and Sodium* for side effects and drug interactions. GI absorption is better than penicillin G. **Note:** Must be taken 1 hr before or 2 hr after meals. Penicillin will prevent rheumatic fever if started within 9 days of the acute illness. **Adjust dose in renal failure (see Chapter 31).****PENTAMIDINE ISETHIONATE**

Pentam 300, NebuPent

**Antibiotic, antiprotozoal**

No



Yes



3



C

**Injection (Pentam 300):** 300 mg**Inhalation (NebuPent):** 300 mg**Treatment:****Pneumocystis jirovecii (carinii):** 4 mg/kg/24 hr IM/IV once daily × 14–21 days

(IV is the preferred route)

**Trypanosomiasis (Trypanosoma gambiense, T. rhodesiense):** 4 mg/kg/24 hr IM once daily × 7 days**Visceral leishmaniasis (Leishmania donovani, L. infantum, L. chagasi):** 4 mg/kg/dose IM once daily, or once every other day × 15–30 doses**Cutaneous leishmaniasis (Leishmania [Viannia] panamensis):** 2–3 mg/kg/dose IM once daily or once every other day × 4–7 doses**Prophylaxis:****Pneumocystis jirovecii (carinii):****IM/IV:** 4 mg/kg/dose Q2–4 wk**Inhalation:****≥5 yr:** 300 mg in 6 mL H<sub>2</sub>O via inhalation Q month. Use with a Respigard II nebulizer.**Max. single dose:** 300 mg

PENTAMIDINE ISETHIONATE *continued*

**Use with caution** in ventricular tachycardia, Stevens-Johnson syndrome, and daily doses >21 days. May cause hypoglycemia, hyperglycemia, hypotension (both IV and IM administration), nausea, vomiting, fever, mild hepatotoxicity, pancreatitis, megaloblastic anemia, nephrotoxicity, hypocalcemia, and granulocytopenia. Additive nephrotoxicity with aminoglycosides, amphotericin B, cisplatin, and vancomycin may occur. Aerosol administration may also cause bronchospasm, cough, oxygen desaturation, dyspnea, and loss of appetite. Infuse IV over 1–2 hr to reduce risk of hypotension. Sterile abscess may occur at IM injection site.

**Adjust dose in renal impairment (see Chapter 31) with systemic use.**

**PENTOBARBITAL**

Nembutal

**Barbiturate**

Yes



No



3



D

**Injection:** 50 mg/mL (20, 50 mL); contains propylene glycol and 10% alcohol

**Hypnotic:****Child:**

**IM:** 2–6 mg/kg/dose; **max. dose:** 100 mg

**Adult:**

**IM:** 150–200 mg

**Preprocedure sedation:****Child:**

**IV/IM:** 3–6 mg/kg/dose; **max. dose:** 150 mg

**Barbiturate coma:****Child and adult:**

**IV, loading dose:** 10–15 mg/kg given slowly over 1–2 hr

**Maintenance:** Begin at 1 mg/kg/hr. **Dose range:** 1–3 mg/kg/hr as needed.

**Contraindicated** in liver failure and history of porphyria. **Use with caution** in hypovolemic shock, CHF, hypotension, and hepatic impairment. No advantage over phenobarbital for control of seizures. Adjunct in treatment of ICP. May cause drug-related isoelectric EEG. **Do not administer** for >2 wk in treatment of insomnia. May cause hypotension, arrhythmias, hypothermia, respiratory depression, and dependence.

Onset of action: IM, 10–15 min; IV, 1 min. Duration of action: IV, 15 min.

Administer IV at a rate of <50 mg/min.

Therapeutic serum levels: Sedation, 1–5 mg/L; hypnosis, 5–15 mg/L; coma, 20–40 mg/L (steady state is achieved after 4–5 days of continuous IV dosing).

**PERMETHRIN**

Elimite, Acticin, Nix, and generics

**Scabicide agent**

No



No



2



B

**Cream (Elimite, Acticin, and generics):** 5% (60 g); contains 0.1% formaldehyde

**Liquid cream rinse (Nix-OTC and generics):** 1% (60 mL with comb); contains 20% isopropyl alcohol

**Lotion [OTC]:** 1% (60 mL with comb)

**Additional permethrin products for use on bedding, furniture, and garments include:**

**Liquid spray (Nix Lice Control Spray):** 0.25% (150 mL)

**Solution (A200 Lice, Rid):** 0.5% (170.1 g or 150 mL)

*Continued*

PERMETHRIN *continued***Pediculus humanus capitis, Phthirus pubis (>2 mo):**

**Head lice:** Saturate hair and scalp with 1% cream rinse after shampooing, rinsing, and towel drying hair. Leave on for 10 min, then rinse. May repeat in 7 days. May be used for lice in other areas of the body (e.g., pubic lice) in same fashion. If the 1% cream rinse is resistant, the 5% cream may be used after shampooing, rinsing, and towel drying hair. Leave on for 8–14 hr overnight under a shower cap, then rinse off. May repeat in 7 days.

**Scabies:** Apply 5% cream from neck to toe (head to toe for infants and toddlers); wash off with water in 8–14 hr. May repeat in 7 days. Use in infants <1 mo is safe and effective when applied for a 6-hr period.

Ovicidal activity generally makes single-dose regimen adequate, but resistance to permethrin has been reported. **Avoid** contact with eyes during application. Shake well before using. May cause pruritus, hypersensitivity, burning, stinging, erythema, and rash. For either lice or scabies, instruct patient to launder bedding and clothing. For lice, treat symptomatic contacts only. For scabies, treat all contacts even if asymptomatic. Topical cream dosage form contains formaldehyde. Dispense 60 g per 1 adult or 2 small children.

**PHENAZOPYRIDINE HCL**

Pyridium, Azo-Standard [OTC], and generics

**Urinary analgesic**



Yes



Yes



3



B

**Tabs:** 95 mg [OTC], 97.2 mg, 100 mg [OTC and Rx], 200 mg

**Oral suspension:** 10 mg/mL

**UTI (use with an appropriate antibacterial agent):**

**Child 6–12 yr:** 12 mg/kg/24 hr ÷ TID PO until symptoms of lower urinary tract irritation are controlled or for 2 days

**Adult:** 95–200 mg TID PO until symptoms are controlled or for 2 days

May cause pruritus, rash, GI distress, vertigo, and headache. Anaphylactoid-like reaction, methemoglobinemia, hemolytic anemia, and renal and hepatic toxicity have been reported, usually at overdosage levels. Colors urine orange; stains clothing. May also stain contact lenses and interfere with urinalysis tests based on spectrometry or color reactions. Give doses after meals.



**Avoid use in moderate/severe renal impairment; adjust dose in mild renal impairment (see Chapter 31).**

**PHENOBARBITAL**

Luminal and generics

**Barbiturate**



Yes



Yes



2



D

**Tabs:** 15, 16.2, 30, 32.4, 60, 64.8, 97.2, 100 mg

**Elixir or oral solution:** 20 mg/5 mL; may contain alcohol

**Injection:** 65, 130 mg/mL; may contain 10% alcohol and propylene glycol

**Status epilepticus:**

**Loading dose, IV:**

**Neonate, infant, and child:** 15–20 mg/kg/dose (**max. loading dose:** 1000 mg) in a single or divided dose. May give additional 5-mg/kg doses Q15–30 min to a **max. total** of 40 mg/kg.

PHENOBARBITAL *continued***Maintenance dose, PO/IV:** Monitor levels.**Neonate:** 3–5 mg/kg/24 hr ÷ once daily–BID**Infant:** 5–6 mg/kg/24 hr ÷ once daily–BID**Child 1–5 yr:** 6–8 mg/kg/24 hr ÷ once daily–BID**Child 6–12 yr:** 4–6 mg/kg/24 hr ÷ once daily–BID**>12 yr:** 1–3 mg/kg/24 hr ÷ once daily–BID**Hyperbilirubinemia (<12 yr):** 3–8 mg/kg/24 hr PO ÷ BID–TID. Doses up to 12 mg/kg/24 hr have been used.**Preoperative sedation (child):** 1–3 mg/kg/dose IM/IV/PO × 1. Give 60–90 min before procedure.**Contraindicated** in porphyria, severe respiratory disease with dyspnea, or obstruction.

**Use with caution** in hepatic or renal disease (reduce dose). IV administration may cause respiratory arrest or hypotension. Side effects include drowsiness, cognitive impairment, ataxia, hypotension, hepatitis, rash, respiratory depression, apnea, megaloblastic anemia, and anticonvulsant hypersensitivity syndrome. Paradoxical reaction in children (not dose related) may cause hyperactivity, irritability, insomnia. Induces several liver enzymes (CYP 450 1A2, 2B6, 2C8, 3A3/4, 3A5–7), thus decreases blood levels of many drugs (e.g., anticonvulsants). **IV push not to exceed 1 mg/kg/min.**

$T_{1/2}$  is variable with age: neonates, 45–100 hr; infants, 20–133 hr; children, 37–73 hr. Owing to long half-life, consider other agents for sedation for procedures.

Therapeutic levels: 15–40 mg/L. Recommended serum sampling time at steady state: trough level obtained within 30 minutes before next scheduled dose after 10–14 days of continuous dosing.

**Adjust dose in renal failure (see Chapter 31).****PHENTOLAMINE MESYLATE**

Regitine (previous brand name), OraVerse, and generics

**Adrenergic blocking agent (alpha); antidote, extravasation**

No



No



?



C

**Injection:** 5 mg vial; may contain mannitol**Injection in solution:** 5 mg/mL (1 mL)**Injection in solution for submucosal use:****OraVerse:** 0.4 mg/1.7 mL (1.7 mL in dental cartridges) (10s, 50s); contains edetate disodium**Treatment of  $\alpha$ -adrenergic drug extravasation (most effective within 12 hr of extravasation):**

All doses are 5 doses administered SC around site of extravasation within 12 hr of extravasation. See table below for weight-based dosing and recommended drug concentration.

Patient Weight	Drug Concentration (diluted with preservative-free NS)	Dose for each syringe 1/5 syringes	Total Dose from all 5 Syringes
<1 kg	0.2 mg/mL	0.05 mL	0.05 mg
1–< 2.5 kg	0.2 mg/mL	0.1 mL	0.1 mg
2.5–< 5 kg	0.2 mg/mL	0.25 mL	0.25 mg
5–< 10 kg	1 mg/mL	0.1 mL	0.5 mg
10–< 20 kg	1 mg/mL	0.2 mL	1 mg
20–< 30 kg	1 mg/mL	0.4 mL	2 mg
30–< 40 kg	1 mg/mL	0.6 mL	3 mg
40–< 50 kg	1 mg/mL	0.8 mL	4 mg
≥50 kg	1 mg/mL	1 mL	5 mg

*Continued*

PHENTOLAMINE MESYLATE *continued***Max. total dose:****Neonate:** 2.5 mg; monitor BP when total dose exceeds 0.1 mg/kg.**Infant, child, adolescent, and adult:** 0.1–0.2 mg/kg/dose or 5 mg**Diagnosis of pheochromocytoma, IM/IV:****Child:** 0.05–0.1 mg/kg/dose up to a **max. dose** of 5 mg**Adult:** 5 mg/dose**Hypertension, before surgery for pheochromocytoma, IM/IV:****Child:** 0.05–0.1 mg/kg/dose up to a **max. dose** of 5 mg 1–2 hr **before** surgery; repeat Q2–4 hr PRN.**Adult:** 5 mg/dose 1–2 hr **before** surgery; repeat Q2–4 hr PRN.**Contraindicated** in MI, coronary insufficiency and angina. **Use with caution** in hypotension, arrhythmias, and cerebral vascular spasm/occlusion.

For diagnosis of pheochromocytoma, patient should be resting in a supine position. A blood pressure reduction of &gt;35 mmHg systolic and 24 mmHg diastolic is considered a positive test for pheochromocytoma. For treatment of extravasation, use 27- to 30-gauge needle with multiple small injections, and monitor site closely because repeat doses may be necessary.

**PHENYLEPHRINE HCL**

Neo-Synephrine, many others, and generics

**Adrenergic agonist**

No



No



3



C

**Injection:** 10 mg/mL (1%) (1, 5, 10 mL); may contain bisulfites**Nasal spray [OTC]:** 0.25, 0.5, 1% (15, 30 mL)**NOTE:** For Neo-Synephrine 12-hr Nasal, see *Oxymetazoline***Ophthalmic drops:** 2.5% (2, 3, 5, 15 mL), 10% (5 mL)**Tabs (Medi-Pheny, Sudafed PE) [OTC]:** 5, 10 mg**Oral solution [OTC]:** 2.5 mg/5 mL (118 mL)**Oral drops [OTC]:** 2.5 mg/1 mL (30 mL)**Hypotension:****NOTE:** IV drip dosage units for children are in mcg/kg/min, compared with mcg/min for adults.

To prepare infusion, see inside front cover.

**Child:****IV bolus:** 5–20 mcg/kg/dose Q10–15 min PRN**IV drip:** 0.1–0.5 mcg/kg/min; titrate to effect**IM/SC:** 0.1 mg/kg/dose Q1–2 hr PRN; **max. dose:** 5 mg**Adult:****IV bolus:** 0.1–0.5 mg/dose Q10–15 min PRN**IV drip:** Initial rate at 100–180 mcg/min; titrate to effect. Usual maintenance dose: 40–60 mcg/min.**IM/SC:** 2–5 mg/dose Q1–2 hr PRN; **max. initial dose:** 5 mg**Pupillary dilation ( $\geq 1$  yr):** 2.5% solution; 1 drop in each eye 15–30 min before examination**Nasal decongestant (in each nostril; give up to 3 days):****Child 6–12 yr:** 2–3 drops or 1–2 sprays of 0.25% solution Q4 hr PRN**>12 yr–adult:** 2–3 drops or 1–2 sprays of 0.25% or 0.5% solution Q4 hr PRN**Oral decongestant (see remarks):****4–<6 yr:****Oral drops (2.5 mg/mL):** 1 mL (2.5 mg) PO Q4 hr; **not to exceed** 6 doses (15 mg) in 24 hr**Oral solution (2.5 mg/5 mL):** 5 mL (2.5 mg) PO Q4 hr, up to 30 mL (15 mg) per 24 hr **$\geq 6$ –<12 yr:****Oral solution (2.5 mg/5 mL):** 10 mL (5 mg) PO Q4 hr up to 60 mL (30 mg) per 24 hr

PHENYLEPHRINE HCL *continued***≥12 yr and adult:****Tabs:** 10–20 mg PO Q4 hr

**Use with caution** in presence of arrhythmias, hyperthyroidism, or hyperglycemia. May cause tremor, insomnia, palpitations. Metabolized by MAO. **Contraindicated** in pheochromocytoma and severe hypertension. Injectable product may contain sulfites.



Nasal decongestants may cause rebound congestion with excessive use (>3 days). The 1% nasal spray can be used in adults with extreme congestion.

Oral phenylephrine is found in a variety of combination cough and cold products and has replaced pseudoephedrine and phenylpropanolamine. Over-the-counter (nonprescription) use of this product is **not recommended** for children <age 6; reports of serious adverse effects (cardiac and respiratory distress, convulsions, and hallucinations) and fatalities (from unintentional overdoses, including combined use of other OTC products containing same active ingredients) have been made.

**PHENYTOIN**

Dilantin, Dilantin Infatab, Phenytek, and generics

**Anticonvulsant, class 1b antiarrhythmic**

Yes



Yes



2



D

**Chewable tabs (Dilantin Infatab and generics):** 50 mg**Prompt-release caps:** 100 mg**Extended-release caps:** 30, 100, 200, 300 mg**Oral suspension:** 125 mg/5 mL (240 mL); contains ≤0.6 % alcohol**Injection:** 50 mg/mL (2, 5 mL); contains alcohol and propylene glycol**Status epilepticus:** see Chapter 1.**Loading dose (all ages):** 15–20 mg/kg IV**Max. dose:** 1500 mg/24 hr**Maintenance for seizure disorders (initiate 12 hr after administration of loading dose):**

**Neonate:** Start with 5 mg/kg/24 hr PO/IV ÷ Q12 hr. Usual range is 4–8 mg/kg/24 hr PO/IV ÷ Q8–12 hr.

**Infant/child:** Start with 5 mg/kg/24 hr ÷ BID–TID PO/IV. Usual dose ranges are (doses divided BID–TID):

**6 mo–3 yr:** 8–10 mg/kg/24 hr

**4–6 yr:** 7.5–9 mg/kg/24 hr

**7–9 yr:** 7–8 mg/kg/24 hr

**10–16 yr:** 6–7 mg/kg/24 hr

**Note:** Use once-daily–BID dosing with extended-release caps.

**Adult:** Start with 100 mg/dose Q8 hr IV/PO and carefully titrate (if needed) by 100-mg increments Q2–4 wk to 300–600 mg/24 hr (or 6–7 mg/kg/24 hr) ÷ Q8–24 hr IV/PO.

**Antiarrhythmic (secondary to digitalis intoxication):****Loading dose (all ages):** 1.25 mg/kg IV Q5 min up to a **total** of 15 mg/kg**Maintenance:**

**Child (IV/PO):** 5–10 mg/kg/24 hr ÷ Q8–12 hr

**Adult:** 250 mg PO QID × 1 day, then 250 mg PO Q12 hr × 2 days, then 300–400 mg/24 hr ÷ Q6–24 hr



**Contraindicated** in patients with heart block or sinus bradycardia, and those who are receiving delavirdine (decrease virologic response). IM administration is **not recommended** because of erratic absorption and pain at injection site; consider fosphenytoin. Side effects include gingival hyperplasia, hirsutism, dermatitis, blood dyscrasia, ataxia, lupus-like and Stevens-Johnson syndromes, lymphadenopathy, liver damage, and nystagmus. Suicidal

*Continued*



PHENYTOIN *continued*

behavior or ideation and multiorgan hypersensitivity (DRESS) have been reported. Increased risk for serious skin reactions (e.g., TEN, Stevens-syndrome) in patients with the HLA-B\*1502 allele.

**Many drug interactions:** Levels may be increased by cimetidine, chloramphenicol, INH, sulfonamides, trimethoprim, etc. Levels may be decreased by some antineoplastic agents. Phenytoin induces hepatic microsomal enzymes (CYP 450 1A2, 2C8/9/19, and 3A3/4), leading to decreased effectiveness of oral contraceptives, fosamprenavir (used without ritonavir), quinidine, valproic acid, theophylline, and other substrates to the previously listed CYP 450 hepatic enzymes. May cause resistance to neuromuscular blocking action of nondepolarizing neuromuscular blocking agents (e.g., pancuronium, vecuronium, rocuronium, and cisatracurium).

**Suggested dosing intervals for specific oral dosage forms:** Extended-release caps, once daily–BID; chewable and immediate-release tablets and oral suspension, TID. Oral absorption reduced in neonates.  $T_{1/2}$  is variable (7–42 hr) and dose dependent. Drug is highly protein bound; free fraction of drug will be increased in patients with hypoalbuminemia.

**For seizure disorders,** therapeutic levels are 10–20 mg/L (free and bound phenytoin) **OR** 1–2 mg/L (free only). Monitor free phenytoin levels in hypoalbuminemia or renal insufficiency. Recommended serum sampling times: trough level (PO/IV) within 30 min before next scheduled dose; peak or post-load level (IV) 1 hr after end of IV infusion. Steady state is usually achieved after 5–10 days of continuous dosing. For routine monitoring, measure trough.

**IV push/infusion rate** **not to exceed** 0.5 mg/kg/min in neonates, or 1 mg/kg/min in infants, children, and adults, with **max.** of 50 mg/min; may cause cardiovascular collapse. Consider fosphenytoin in situations of tenuous IV access and risk for extravasation.

**PHOSPHORUS SUPPLEMENTS**

K-PHOS Neutral, Phospha 250 Neutral, PHOS-NaK, Sodium Phosphate, Potassium Phosphate, and many generics for injection



No



Yes



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C

**Oral:** (Reconstitute in 75 mL H<sub>2</sub>O per tablet or packet of powder.)

**Na and K phosphate:**

**PHOS-NaK, powder [OTC]:** 250 mg (8 mM) P, 6.96 mEq (160 mg) Na, 7.16 mEq (280 mg) K per packet of powder (100s)

**K-PHOS Neutral or Phospha 250 Neutral, tabs:** 250 mg P (8 mM), 13 mEq Na, 1.1 mEq K

**K-PHOS No. 2, tabs:** 250 mg P (8 mM), 5.8 mEq Na, 2.3 mEq K

**Injection:**

**Na phosphate:** 3 mM (93 mg) P, 4 mEq Na/mL

**K phosphate:** 3mM (93 mg) P, 4.4 mEq K/mL

Conversion: 31 mg P = 1 mM P

**Acute hypophosphatemia:** 0.16–0.32 mM/kg/dose (or 5–10 mg/kg/dose) IV over 6 hr

**Maintenance/replacement:****Child:**

**IV:** 0.5–1.5 mM/kg (or 15–45 mg/kg) over 24 hr

**PO:** 30–90 mg/kg/24 hr (or 1–3 mM/kg/24 hr) ÷ TID–QID

**Adult:**

**IV:** 50–65 mM (or 1.5–2 g) over 24 hr

**PO:** 3–4.5 g/24 hr (or 100–150 mM/24 hr) ÷ TID–QID

**Recommended IV infusion rate:** ≤0.1 mM/kg/hr (or 3.1 mg/kg/hr) of phosphate. When potassium salt is used, the rate will be limited by the **max.** potassium infusion rate. **Do not** co-infuse with calcium-containing products.



PHOSPHORUS SUPPLEMENTS *continued*

May cause tetany, hyperphosphatemia, hyperkalemia, hypocalcemia. **Use with caution** in patients with renal impairment. Be aware of sodium and/or potassium load when supplementing phosphate. IV administration of potassium-salt product may cause hypotension, renal failure, arrhythmias, heart block, or cardiac arrest. PO dosing may cause nausea, vomiting, abdominal pain, or diarrhea. See Chapter 21 for daily requirements and Chapter 11 for additional information on hypophosphatemia and hyperphosphatemia.

**PHYSOSTIGMINE SALICYLATE**

Antilirium (former brand name) and generics

**Cholinergic agent**

No



No



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**Injection:** 1 mg/mL (2 mL); contains 2% benzyl alcohol and 0.1% sodium bisulfite

**Reversal of toxic anticholinergic effects from antihistamine or anticholinergic agents:**

**Child:** 0.01–0.03 mg/kg/dose IV administered over 3–5 min. Dose may be repeated

Q20 min if no response or return of anticholinergic symptoms up to a **max. total** of 2 mg.

**Adult:** 0.5–2 mg IV (administered over 5 min)/IM/SC. If needed, repeat dose Q20 min until response is seen or when adverse effects occur.

**Physostigmine antidote:** Atropine always should be available. **Contraindicated** in asthma, gangrene, diabetes, cardiovascular disease, GI or GU tract obstruction, any vagotonic state, and patients receiving choline esters or depolarizing neuromuscular blocking agents (e.g., decamethonium, succinylcholine). May cause seizures, arrhythmias, bradycardia, GI symptoms, and other cholinergic effects. Rapid IV administration can cause bradycardia and hypersalivation leading to respiratory distress and seizures.



Pregnancy code not formally assigned by the FDA.

**PHYTONADIONE/VITAMIN K<sub>1</sub>**

Mephyton and generics

**Vitamin, fat soluble**

No



No



2



C

**Tabs (Mephyton):** 5 mg

**Oral suspension:** 1 mg/mL 

**Injection, emulsion:**

2 mg/mL (0.5 mL); preservative free

10 mg/mL (1 mL); contains 0.9% benzyl alcohol

**Neonatal hemorrhagic disease (vitamin K deficiency bleeding):**

**Prophylaxis:** 0.5–1 mg IM × 1 within 1 hr after birth

**Treatment:** 1–2 mg/24 hr IM/SC/IV

**Oral anticoagulant (warfarin) overdose (see remarks):**

**INR ≥ 5 and no serious bleeding:**

<40 kg: 30 mcg/kg PO/IV

≥40 kg: 1–2.5 mg PO/IV

**Suggested INR monitoring schedule:**

**INR 5–8:** Q12–24 hr

**INR ≥ 8:** Q6–12 hr and repeat dose if necessary

Continued

PHYTONADIONE/VITAMIN K<sub>1</sub> *continued*

**Serious bleeding (any elevated INR):** 2.5–5 mg PO/IV and monitor INR Q6 hr and repeat dose if necessary.

**Life-threatening bleeding (any elevated INR):** 5–10 mg PO/IV and monitor INR Q2–4 hr and repeat dose if necessary. Consider the use of FFP.

**Vitamin K deficiency:****Infant and child:**

**PO:** 2.5–5 mg/24 hr

**IM/SC/IV:** 1–2 mg/dose × 1

**Adolescent and adult:**

**PO:** 2.5–25 mg/24 hr

**IM/SC/IV:** 2.5–10 mg/dose × 1

Monitor PT/PTT. Large doses (10–20 mg) in newborns may cause hyperbilirubinemia and severe hemolytic anemia. Blood coagulation factors increase within 6–12 hr after oral doses and within 1–2 hr after parenteral administration.

IV injection rate **not to exceed** 3 mg/m<sup>2</sup>/min or 1 mg/min. IV or IM doses may cause flushing, dizziness, cardiac/respiratory arrest, hypotension, and anaphylaxis. IV or IM administration is indicated only when other routes of administration are not feasible (or in emergency situations). Concurrent administration of oral mineral oil may decrease GI absorption of oral vitamin K. Protect product from light. See Chapter 21 for multivitamin preparations.

**PILOCARPINE HCL**

Isopto Carpine, Salagen, Pilopine HS, and others

**Cholinergic agent**

Yes



No



3



C

**Ophthalmic solution (Isopto Carpine and generics):** 1% (15 mL), 2% (15 mL), 4% (15 mL); may contain benzalkonium chloride

**Ophthalmic gel (Pilopine HS):** 4% (4 g); contains benzalkonium chloride

**Tab (Salagen and others):** 5, 7.5 mg

**For elevated intraocular pressure:****Child and adult:**

**Drops:** 1–2 drops in each eye 4–6 times a day; adjust concentration and frequency as needed.

**Gel:** 0.5-inch ribbon applied to lower conjunctival sac QHS. Adjust dose as needed.

**Xerostomia:**

**Adult:** 5 mg/dose PO TID; dose may be titrated to 10 mg/dose PO TID in patients who do not respond to lower dose and who are able to tolerate the drug. 5 mg/dose PO QID has been used in Sjögren syndrome.

**OPHTHALMIC USE: Contraindicated** in acute iritis or anterior chamber inflammation and uncontrolled asthma. May cause stinging, burning, lacrimation, headache, and retinal detachment. **Use with caution** in patients with corneal abrasion or significant cardiovascular disease. Use with topical NSAIDs (e.g., ketorolac) may decrease topical pilocarpine effects.

**ORAL USE:** Sweating, nausea, rhinitis, chills, flushing, urinary frequency, dizziness, asthenia, and headaches have also been reported. Reduce oral dosing in the presence of mild hepatic insufficiency (Child-Pugh score of 5–6); use in severe hepatic insufficiency is **not recommended**.

**PIMECROLIMUS**

Elidel

*Topical immunosuppressant*

No



No



3



C

**Cream:** 1% (30, 60, 100 g); contains benzyl alcohol and propylene glycol**Atopic dermatitis (second-line therapy):****≥2 yr and adult (see remarks):** Apply a thin layer to affected area BID and rub in gently and completely. Reevaluate patient in 6 wk if lesions are not healed.**Do not use** in children <2 (higher rate of upper respiratory infections), immunocompromised patients, or with occlusive dressings (promotes systemic absorption). Approved as a second-line therapy for atopic dermatitis for patients who fail to respond or do not tolerate other approved therapies. Use medication for short periods of time by using the minimal amounts to control symptoms; long-term safety is unknown. **Avoid** contact with eyes, nose, mouth, and cut, infected, or scraped skin. Minimize and **avoid** exposure to natural and artificial sunlight, respectively.Most common side effects include burning at application site, headache, viral infections, and pyrexia. Skin discoloration, skin flushing associated with alcohol use, anaphylactic reactions, ocular irritation after application to eyelids or near eyes, angioneurotic edema, and facial edema have been reported. Although risk is uncertain, the FDA has issued an alert about potential cancer risk with use of this product. See [www.fda.gov/medwatch](http://www.fda.gov/medwatch) for latest information. Drug is a CYP 450 3A3/4 substrate.**PIPERACILLIN WITH TAZOBACTAM**

Zosyn and generics

*Antibiotic, penicillin (extended spectrum with  $\beta$ -lactamase inhibitor)*

No



Yes



2



B

**8:1 ratio of piperacillin to tazobactam:****Injection, powder:** 2 g piperacillin and 0.25 g tazobactam; 3 g piperacillin and 0.375 g tazobactam; 4 g piperacillin and 0.5 g tazobactam; 36 g piperacillin and 4.5 g tazobactam**Injection, premixed in iso-osmotic dextrose:** 2 g piperacillin and 0.25 g tazobactam in 50 mL; 3 g piperacillin and 0.375 g tazobactam in 50 mL; 4 g piperacillin and 0.5 g tazobactam in 100 mL

Contains 2.79 mEq Na/g piperacillin

**All doses based on piperacillin component.****Neonate:** 100 mg/kg/dose IV at the following intervals:**<1 kg:****≤14 days old:** Q12 hr**15–28 days old:** Q8 hr**≥1 kg:****≤7 days old:** Q12 hr**8–28 days old:** Q8 hr**Severe infections (IV; shortening the dosing interval to Q6 hr and lengthening the dose administration time (see remarks) may enhance the pharmacodynamic properties):****<2 mo (currently undefined by manufacturer; extrapolated from piperacillin dosing):** 300–400 mg/kg/24 hr ÷ Q6 hr**2–9 mo:** 240 mg/kg/24 hr ÷ Q8 hr**>9 mo:** 300 mg/kg/24 hr ÷ Q8 hr; **max. dose:** 16 g/24 hr

Continued

PIPERACILLIN WITH TAZOBACTAM *continued*

**Appendicitis or peritonitis (IV route for 7–10 days; dosing interval may be shortened to Q6 hr to enhance pharmacodynamic properties):**

**2–9 mo:** 240 mg/kg/24 hr ÷ Q8 hr

**>9 mo–adolescent and ≤40 kg:** 300 mg/kg/24 hr ÷ Q8 hr

**>9 mo–adolescent and >40 kg:** 3 g Q6 hr; **max. dose:** 16 g/24 hr

**Adult:**

**Intraabdominal or soft-tissue infections:** 3 g IV Q6 hr

**Nosocomial pneumonia:** 4 g IV Q6 hr

**Cystic fibrosis (antipseudomonal):** 350–600 mg/kg/24 hr IV ÷ Q4–6 hr; **max. dose:** 24 g/24 hr

Tazobactam is a  $\beta$ -lactamase inhibitor, thus extending the spectrum of piperacillin. Like other penicillins, CSF penetration occurs only with inflamed meninges. GI disturbances, pruritus, rash, and headaches are common. Abnormal platelet aggregation and prolonged bleeding, serious skin reactions (e.g., Stevens-Johnson syndrome, TEN) have been reported in patients with renal failure. Cystic fibrosis patients have an increased risk for fever and rash.

Coagulation parameters should be tested more frequently and monitored regularly with high doses of heparin, warfarin, or other drugs affecting blood coagulation or thrombocyte function. May falsely decrease aminoglycoside serum levels if the drugs are infused close to one another; allow a minimum of 2 hours between infusions to prevent this interaction. May prolong the neuromuscular blockade effects of vecuronium.

Prolonging the dose administration time to 4 hr will maximize the pharmacokinetic/pharmacodynamic properties by prolonging the time of drug concentration above the MIC. **Adjust dose in renal impairment (see Chapter 31).**

**POLYCITRA**

See Citrate Mixtures

**POLYETHYLENE GLYCOL—ELECTROLYTE SOLUTION**

Bowel cleansing products: GoLYTELY, CoLyte, NuLYTELY, TriLyte, and generics

Laxative products: MiraLax, Dulcolax Balance, and generics

**Bowel evacuant, osmotic laxative**



No



No



?



C

**Powder for oral solution:**

GoLYTELY and others: Polyethylene glycol 3350 236 g, Na sulfate 22.74 g, Na bicarbonate 6.74 g, NaCl 5.86 g, KCl 2.97 g (mixed with water to 4 L). Contents vary somewhat. See package insert for specific contents of other products.

MiraLax (OTC), Dulcolax Balance (OTC), and others: Polyethylene glycol 3350 (17, 119, 238, 250, 255, 500, 510, 527, 850 g)

**Bowel cleansing (use products containing supplemental electrolytes for bowel cleansing, such as GoLYTELY, CoLyte, NuLYTELY, TriLyte and others; patients should be NPO 3–4 hr before dosing):**

**Child:**

**Oral/nasogastric:** 25–40 mL/kg/hr until rectal effluent is clear (usually in 4–10 hr)

**Adult:**

**Oral:** 240 mL PO Q10 min up to 4 L or until rectal effluent is clear

**Nasogastric:** 20–30 mL/min (1.2–1.8 L/hr) up to 4 L

PHYTONADIONE/VITAMIN K<sub>1</sub> *continued***Constipation (MiraLax, Dulcolax Balance, and others):**

**Child (limited data in 20 children with chronic constipation, 18 mo–11 yr; see remarks):** A mean effective dose of 0.84 g/kg/24 hr PO ÷ BID for 8 wk (range, 0.25–1.42 g/kg/24 hr) was used to yield 2 soft stools per day. Do not exceed 17 g/24 hr. If patient > 20 kg, use adult dose.

**Adult:** 17 g (one heaping tablespoonful) mixed in 240 mL of water, juice, soda, coffee, or tea PO once daily

**Fecal impaction (MiraLax, Dulcolax Balance, and others):**

>3 yr: 1–1.5 g/kg/24 hr (**max. dose:** 100 g/24 hr) PO × 3 days

**Contraindicated** in polyethylene glycol hypersensitivity. Monitor electrolytes, BUN, serum glucose, and urine osmolality with prolonged administration. Seizures resulting from electrolyte abnormalities have been reported.



**BOWEL CLEANSING: Contraindicated** in toxic megacolon, gastric retention, colitis, and bowel perforation. **Use with caution** in patients prone to aspiration or with impaired gag reflex. Effect should occur within 1–2 hr. Solution generally more palatable if chilled.

**CONSTIPATION (MiraLax and others): Contraindicated** in bowel obstruction

**Child:** Dilute powder using the ratio of 17 g powder to 240 mL of water, juice, or milk. Onset of action within 1 wk in 12 of 20 patients, with remaining 8 patients reporting improvement during second wk of therapy. Side effects reported in this trial included diarrhea, flatulence, and mild abdominal pain. (See *J Pediatr* 2001;139:428–432 for additional information.)

**Adult:** 2 to 4 days may be required to produce a bowel movement. Most common side effects include nausea, abdominal bloating, cramping, and flatulence. Use beyond 2 wk has not been studied.

## POLYMYXIN B SULFATE AND BACITRACIN

See Bacitracin ± Polymyxin B

## POLYMYXIN B SULFATE AND TRIMETHOPRIM SULFATE

Polytrim Ophthalmic Solution and various others

**Topical antibiotic (ophthalmic preparations listed)**



No



No



2



C

**Ophthalmic solution:** Polymyxin B sulfate 10,000 U, trimethoprim sulfate 1 mg/mL (10 mL); some preparations may contain 0.04 mg/mL benzalkonium chloride.

≥2 mo and adult: Instill 1 drop in affected eye(s) Q3 hr (**max.** of 6 doses/24 hr) × 7–10 days.



Active against susceptible strains of *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus pneumoniae*, *Streptococcus viridans*, *Haemophilus influenzae*, and *Pseudomonas aeruginosa*. **Not indicated** for prophylaxis or treatment of ophthalmia neonatorum. Local irritation consisting of redness, burning, stinging, and/or itching is common. Hypersensitivity reactions consisting of lid edema, itching, increased redness, tearing, and/or circumocular rash have been reported.

Apply finger pressure to lacrimal sac during and for 1–2 min after dose application.



**POLYMYXIN B SULFATE, NEOMYCIN SULFATE, HYDROCORTISONE**

Cortisporin Otic, AK-Spore H.C. Otic, PediOtic, and generics

**Topical antibiotic (otic and ophthalmic preparations listed)**

No



No



2



C

**Otic solution or suspension:** Polymyxin B sulfate 10,000 U, neomycin sulfate 5 mg (3.5 mg neomycin base), hydrocortisone 10 mg/mL (10 mL); some preparations may contain thimerosal and metabisulfite.

**Ophthalmic suspension:** Polymyxin B sulfate 10,000 U, neomycin sulfate 5 mg (3.5 mg neomycin base), hydrocortisone 10 mg/mL (7.5 mL); may contain thimerosal and propylene glycol.

**Otitis externa:**

≥2 yr—**adult:** 3–4 drops TID–QID × 7–10 days. If preferred, a cotton wick may be saturated and inserted into ear canal. Moisten wick with antibiotic Q4 hr. Change wick Q24 hr.

**Ophthalmic:**

**Child, adolescent and adult:** Instill 1–2 drops into affected eye(s) Q3–4 hr.

Neomycin may cause sensitization. Prolonged treatment may result in overgrowth of nonsusceptible organisms and fungi. May cause cutaneous sensitization.

**OTIC USE:** Shake suspension well before use. **Contraindicated** in patients with active varicella and herpes simplex and in cases with perforated eardrum (possible ototoxicity).

**Use with caution** in chronic otitis media and when integrity of tympanic membrane is in question. Metabisulfite-containing products may cause allergic reactions to susceptible individuals. Hypersensitivity (itching, skin rash, redness, swelling, or other sign of irritation in or around ear) may occur. Warm medication to body temperature before use.

**OPHTHALMIC USE:** **Use with caution** in glaucoma. Blurred vision, burning, and stinging may occur. Increased intraocular pressure and mycosis may occur with prolonged use. Apply finger pressure to lacrimal sac during and for 1–2 min after dose application.

**POLYTRIM OPHTHALMIC SOLUTION**

See Polymyxin B Sulfate and Trimethoprim Sulfate

**POTASSIUM IODIDE**

Iosat, SSKI, ThyroShield, ThyroSafe, and others

**Antithyroid agent**

No



Yes



X



D

**Tabs:**

**Iosat [OTC]:** 65 mg (50 mg iodine), 130 mg

**ThyroSafe [OTC]:** 65 mg

**Oral solution:**

**ThyroShield [OTC]:** 65 mg/mL (30 mL); contains parabens and saccharin

**Saturated solution (SSKI):** 1000 mg/mL (30, 240 mL); 10 drops = 500 mg potassium iodide  
Potassium content is 6 mEq (234 mg) K<sup>+</sup>/g potassium iodide.

**Neonatal Grave's disease:** 50–100 mg (about 1–2 drops of SSKI) PO once daily

**Thyrotoxicosis:**

**Child:** 50–250 mg (about 1–5 drops of SSKI) PO TID

**Adult:** 50–500 mg (1–10 drops of SSKI) PO TID

POTASSIUM IODIDE *continued*

**Cutaneous or lymphocutaneous sporotrichosis (treat for 4–6 wk after lesions have completely healed; increase dose until either max. dose is achieved or signs of intolerance appear):**

**Child and adult:** Start with 250 mg PO TID. Doses may be gradually increased as tolerated to the following **max. doses**:

**Child max. dose:** 1250–2000 mg PO TID

**Adult max. dose:** 2000–2500 mg PO TID

**Contraindicated** in pregnancy, hyperkalemia, iodine-induced goiter, and hypothyroidism. **Use with caution** in cardiac disease and renal failure. GI disturbance, metallic taste, rash, salivary gland inflammation, headache, lacrimation, and rhinitis are symptoms of iodism. Give with milk or water after meals. Monitor thyroid function tests. Onset of antithyroid effects: 1–2 days.



Lithium carbonate and iodide-containing medications may have synergistic hypothyroid activity.

Potassium-containing medications, potassium-sparing diuretics, and ACE inhibitors may increase serum potassium levels.

For use as a thyroid blocking agent in radiation emergencies, see [www.fda.gov/cder/guidance/4825fnl.pdf](http://www.fda.gov/cder/guidance/4825fnl.pdf).

## PORACTANT ALFA

See Surfactant, pulmonary

## POTASSIUM SUPPLEMENTS

Many brand names and generics

**Electrolyte**



No



Yes



1



C

**Potassium chloride (40 mEq K = 3 g KCl):**

**Sustained-release caps:** 8, 10 mEq

**Sustained-release tabs:** 8, 10, 15, 20 mEq

**Powder:** 20, 25 mEq/packet

**Oral solution/liquid:** 10% (6.7 mEq/5 mL), 20% (13.3 mEq/5 mL)

**Concentrated injection:** 2 mEq/mL

**Potassium gluconate (40 mEq K = 9.4 g K gluconate):**

**Tabs:** 465 mg (2 mEq), 581 mg (2.5 mEq)

**Caps [OTC as K-99]:** 595 mg (2.56 mEq)

**Potassium acetate (40 mEq K = 3.9 g K acetate):**

**Concentrated injection:** 2, 4 mEq/mL

**Potassium bicarbonate (10 mEq K = 1 g K bicarbonate):**

**Caps:** 99 mg

**Effervescent tab for oral solution:** 25 mEq

**Potassium phosphate:**

See *Phosphorus Supplements*.

**Normal daily requirements:** See Chapter 21.

**Replacement:** Determine based on maintenance requirements, deficit, and ongoing losses.

See Chapter 11.

**Hypokalemia:**

**Oral:**

**Child:** 1–4 mEq/kg/24 hr ÷ BID–QID. Monitor serum potassium.

**Adult:** 40–100 mEq/24 hr ÷ BID–QID



*Continued*



POTASSIUM SUPPLEMENTS *continued***Hypokalemia (cont.)****IV: CLOSELY MONITOR SERUM K.****Child:** 0.5–1 mEq/kg/dose given as an infusion of 0.5 mEq/kg/hr  $\times$  1–2 hr**Max. IV infusion rate:** 1 mEq/kg/hr. This may be used in critical situations (i.e., hypokalemia with arrhythmia).**Adult:****Serum K  $\geq$  2.5 mEq/L:** Replete at rates up to 10 mEq/hr. **Total dosage not to exceed** 200 mEq/24 hr.**Serum K < 2 mEq/L:** Replete at rates up to 40 mEq/hr. **Total dosage not to exceed** 400 mEq/24 hr.**Max. peripheral IV solution concentration:** 40 mEq/L**Max. concentration for central line administration:** 150–200 mEq/L

PO administration may cause GI disturbance and ulceration. Oral liquid supplements should be diluted in water or fruit juice before administration. Sustained-release tablets must be swallowed whole and **NOT** dissolved in the mouth or chewed.



**Do not administer** IV potassium undiluted. IV administration may cause irritation, pain, and phlebitis at infusion site. **Rapid or central IV infusion may cause cardiac arrhythmias.** Patients receiving infusion > 0.5 mEq/kg/hr (>20 mEq/hr for adults) should be placed on ECG monitor.

**PRALIDOXIME CHLORIDE****Protopam, 2-PAM, and generics**

In combination with atropine: Duodote

**Antidote, organophosphate poisoning**

No



Yes



?



C

**Injection:** 1000 mg**Injection for intramuscular injection, in auto-injector device:** 600 mg/2 mL (2 mL); dispenses 600 mg; contains benzyl alcohol**In combination with atropine (Duodote):** 600 mg/2 mL of pralidoxime and 2.1 mg/0.7 mL of atropine. Duodote must be administered by emergency medical services personnel who have had adequate training in recognition and treatment of nerve agent or insecticide intoxication.**Organophosphate poisoning (use with atropine):****Child:****IV:** 20–50 mg/kg/dose (**max. dose:** 2000 mg)  $\times$  1 IV. May repeat in 1–2 hr if muscle weakness is not relieved, then at Q10–12 hr PRN if cholinergic signs reappear.**IV continuous infusion:** Loading dose of 20–50 mg/kg/dose (**max. dose:** 2000 mg) IV over 15–30 min, followed by 10–20 mg/kg/hr.**IM:****<40 kg:** 15 mg/kg/dose  $\times$  1 IM. May repeat Q15 min PRN up to a **max. total dose** of 45 mg/kg for mild symptoms. May repeat twice in rapid succession for severe symptoms (**max. total dose** of 45 mg/kg). For persistent symptoms, may repeat another **max.** 45 mg/kg series (in 3 divided doses)  $\approx$  1 hr after last injection. **$\geq$ 40 kg:** 600 mg  $\times$  1 IM. May repeat Q15 min PRN up to a **max. total dose** of 1800 mg for mild symptoms. May repeat twice in rapid succession for severe symptoms (**max. total dose** of 1800 mg). For persistent symptoms, may repeat another **max.** 1800 mg series (in 3 divided doses)  $\approx$  1 hr after last injection.

PRALIDOXIME CHLORIDE *continued***Adult:**

**IV:** 1–2 g/dose  $\times$  1 IV. May repeat in 1–2 hr if muscle weakness is not relieved, then at Q10–12 hr PRN if cholinergic signs reappear.

**IM:** Use  $\geq 40$  kg child IM dosage from above.

**Contraindicated** in poisonings due to phosphorus, inorganic phosphates, or organic phosphates without anticholinesterase activity. **Do not use** as an antidote for carbamate classes of pesticides. Removal of secretions and maintaining a patent airway is critical. May cause muscle rigidity, laryngospasm, and tachycardia after rapid IV infusion. Drug is generally ineffective if administered 36–48 hr after exposure. Additional doses may be necessary.

For IV administration, dilute to 50 mg/mL or less, and infuse over 15–30 min (**not to exceed** 200 mg/min). Reduce dosage in renal impairment, since 80%–90% of drug is excreted unchanged in urine 12 hr after administration.

**PREDNISOLONE****Oral products:**

Orapred, Orapred ODT, Prelone, Pediapred, Millipred, Veripred 20, and generics

**Ophthalmic products:**

Pred Forte, Pred Mild, Omnipred, and generics

**Corticosteroid**

No



No



2



C/D

**Tabs:** 5 mg

**Syrup (Prelone and generics):** 15 mg/5 mL (240 mL); may contain alcohol and saccharin

**Tablets, orally disintegrating (as Na phosphate) (Orapred ODT):** 10, 15, 30 mg

**Oral solution (as Na phosphate):**

**Pediapred and generics:** 5 mg/5 mL (120 mL); alcohol and dye free

**Orapred and generics:** 15 mg/5 mL (237 mL); may contain 2% alcohol and is dye free

**Millipred:** 10 mg/5 mL (237 mL); contains parabens and is dye free

**Veripred 20:** 20 mg/5 mL (237 mL); alcohol and dye free; and contains parabens

**Ophthalmic suspension (as acetate):** 0.12% (5, 10 mL), 1% (5, 10, 15 mL); contains benzalkonium chloride and may contain bisulfites

**Ophthalmic solution (as Na phosphate):** 1% (10 mL); may contain benzalkonium chloride

See *Prednisone* (equivalent dosing).

**Ophthalmic (consult ophthalmologist before use):**

**Child and adult:** Start with 1–2 drops Q1 hr during the day and Q2 hr during the night until favorable response, then reduce dose to 1 drop Q4 hr. Dose may be further reduced to 1 drop TID–QID.

See *Prednisone* for remarks. See Chapter 30 for relative steroid potencies. Pregnancy category changes to "D" if used in first trimester. Orapred oral solution product should be stored in refrigerator.

**OPHTHALMIC USE:** **Contraindicated** in viral (e.g., herpes simplex, vaccinia and varicella), fungal, and mycobacterial infections of cornea and conjunctiva. Increase in intraocular pressure, cataract formation, and delayed wound healing may occur.

**PREDNISONE**

Orasone, Deltasone, Liquid Pred, Rayos, and generics

**Corticosteroid**

Yes



No



2



C/D

**Tabs:** 1, 2.5, 5, 10, 20, 50 mg**Delayed-release tabs (Rayos):** 1, 2, 5 mg**Oral solution:** 1 mg/mL (120, 500 mL); may contain 5% alcohol and saccharin**Concentrated solution:** 5 mg/mL (30 mL); contains 30% alcohol**Antiinflammatory/immunosuppressive:****Child:** 0.5–2 mg/kg/24 hr PO ÷ once daily–BID**Acute asthma:****Child:** 2 mg/kg/24 hr PO ÷ once daily–BID × 5–7 days. **Max. dose:** 80 mg/24 hr. Patients may benefit from tapering if therapy exceeds 5–7 days.**Asthma exacerbations (2007 National Heart, Lung, and Blood Institute Guideline Recommendations; dose until peak expiratory flow reaches 70% of predicted or personal best):****Child ≤ 12 yr:** 1–2 mg/kg/24 hr PO ÷ Q12 hr (**max. dose:** 60 mg/24 hr)**>12 yr and adult:** 40–80 mg/24 hr PO ÷ Q12–24 hr**Outpatient asthma exacerbation burst therapy (longer durations may be necessary):****Child ≤ 12 yr:** 1–2 mg/kg/24 hr PO ÷ Q12–24 hr (**max. dose:** 60 mg/24 hr) × 3–10 days**Child > 12 yr and adult:** 40–60 mg/24 hr PO ÷ Q12–24 hr × 5–10 days**Nephrotic syndrome:****Child:** Starting dose of 2 mg/kg/24 hr PO (**max. dose:** 80 mg/24 hr) ÷ once daily–TID is recommended. Further treatment plans are individualized. Consult a nephrologist.

See Chapter 30 for physiologic replacement, relative steroid potencies, and doses based on body surface area. Methylprednisolone is preferable in hepatic disease, because prednisone must be converted to methylprednisolone in the liver.

Side effects may include mood changes, seizures, hyperglycemia, diarrhea, nausea, abdominal distension, GI bleeding, HPA axis suppression, osteopenia, cushingoid effects, and cataracts with prolonged use. Prednisone is a CYP 450 3A3/4 substrate and inducer. Barbiturates, carbamazepine, phenytoin, rifampin, and isoniazid may reduce effects of prednisone, whereas estrogens may enhance effects. Pregnancy category changes to "D" if used in first trimester.

**PRIMAQUINE PHOSPHATE**

Various generic brands

**Antimalarial**

No



No



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C

**Tabs:** 26.3 mg (15 mg base)**Oral suspension:** 10.52 mg (6 mg base)/5 mL **Doses expressed in mg of primaquine base.****Malaria:****Prevention of relapses for Plasmodium vivax or Plasmodium ovale only (initiate therapy during last 2 wk of, or after a course of, suppression with chloroquine or comparable drug):****Child:** 0.5 mg/kg/dose (**max. dose:** 30 mg/dose) PO once daily × 14 days**Adult:** 30 mg PO once daily × 14 days**Prevention of chloroquine-resistant strains (initiate 1 day before departure and continue until 3–7 days after leaving endemic area):****Child:** 0.5 mg/kg/dose PO once daily; **max. dose:** 30 mg/24 hr**Adult:** 30 mg PO once daily

PRIMAQUINE PHOSPHATE *continued***Pneumocystis jirovecii (carinii) pneumonia (in combination with clindamycin):****Child:** 0.3 mg/kg/dose (**max. dose:** 30 mg/dose) PO once daily × 21 days**Adult:** 30 mg PO once daily × 21 days

**Contraindicated** in granulocytopenia (e.g., rheumatoid arthritis, lupus erythematosus) and bone marrow suppression. **Avoid use** with quinacrine and other drugs that have a potential for causing hemolysis or bone marrow suppression. **Use with caution** in G6PD and NADH methemoglobin reductase-deficient patients; increased risk for hemolytic anemia and leukopenia, respectively. Use in pregnancy is **not recommended** by the AAP *Red Book*. Cross-sensitivity with iodoquinol.

May cause headache, visual disturbances, nausea, vomiting, and abdominal cramps. Hemolytic anemia, leukopenia, and methemoglobinemia have been reported. Administer all doses with food to mask bitter taste.

**PRIMIDONE**

Mysoline and generics

**Anticonvulsant, barbiturate**

Yes



Yes



2



D

**Tabs:** 50, 250 mg

**Neonate:** 12–20 mg/kg/24 hr PO ÷ BID–QID. Initiate therapy at the lower dosage range and titrate upwards.

**Child, adolescent, and adult:**



Day of Therapy	<8 yr	≥8 yr and Adult
Days 1–3	50 mg PO QHS	100–125 mg PO QHS
Days 4–6	50 mg PO BID	100–125 mg PO BID
Days 7–9	100 mg PO BID	100–125 mg PO TID
Day 10 and thereafter	125–250 mg PO TID or 10–25 mg/kg/ 24 hr ÷ TID–QID	250 mg PO TID–QID; max. dose: 2 g/24 hr

**Use with caution** in renal or hepatic disease and pulmonary insufficiency. Primidone is metabolized to phenobarbital and has the same drug interactions and toxicities (see *Phenobarbital*). Additionally, primidone may cause vertigo, nausea, leukopenia, malignant lymphoma-like syndrome, diplopia, nystagmus, and systemic lupus-like syndrome. Monitor for suicidal behavior or ideation. Acetazolamide may decrease primidone absorption. **Adjust dose in renal failure (see Chapter 31).**



Follow both primidone and phenobarbital levels. Therapeutic levels: 5–12 mg/L of primidone and 15–40 mg/L of phenobarbital. Recommended serum sampling time at steady state: trough level obtained within 30 min before next scheduled dose after 1–4 days of continuous dosing.

**PROBENECID**

Various generic brands

**Penicillin therapy adjuvant, uric acid–lowering agent**

No



Yes



?



B

**Tabs:** 500 mg**To prolong penicillin levels:****Child (2–14 yr):** 25 mg/kg PO  $\times$  1, then 40 mg/kg/24 hr  $\div$  QID. **Max. single dose:**500 mg/dose. Use adult dose if  $>50$  kg.**Adult:** 500 mg PO QID**Hyperuricemia:****Adult:** 250 mg PO BID  $\times$  1 wk, then 500 mg PO BID. May increase by 500-mg increments Q4 wk PRN up to a **max. dose** of 2–3 g/24 hr  $\div$  BID.**Gonorrhea, antibiotic adjunct (just before antibiotic):** **$\leq 45$  kg:** 23 mg/kg/dose PO  $\times$  1 just before antibiotic **$>45$  kg:** 1 g PO  $\times$  1**Use with caution** in patients with peptic ulcer disease. **Contraindicated** in children  $<2$  yr and patients with renal insufficiency. **Do not use** if GFR  $< 30$  mL/min.

Increases uric acid excretion. Inhibits renal tubular secretion of acyclovir, ganciclovir, ciprofloxacin, levofloxacin, nalidixic acid, moxifloxacin, organic acids, penicillins, cephalosporins, AZT, dapsone, methotrexate, NSAIDs, and benzodiazepines. Salicylates may decrease probenecid's activity. Alkalinize urine in patients with gout. May cause headache, GI symptoms, rash, anemia, and hypersensitivity. False-positive glucosuria with Clinitest may occur.

**PROCAINAMIDE**

Various generic brands

**Antiarrhythmic, class Ia**

Yes



Yes



X



C

**Injection:** 500 mg/mL (2, 10 mL); may contain methylparabens and bisulfites**Child:****V. tach with poor perfusion:** Consider 15 mg/kg/dose IV  $\times$  1 over 30–60 min if cardioversion ineffective. Follow with continuous infusion if effective (see information that follows).**IM:** 20–30 mg/kg/24 hr  $\div$  Q4–6 hr; **max. dose:** 4 g/24 hr (peak effect in 1 hr)**IV: Loading:** 3–6 mg/kg/dose over 5 min (**max. dose:** 100 mg/dose). Repeat dose Q5–10 min PRN up to a **total max. dose** of 15 mg/kg. **Do not exceed** 500 mg in 30 min.**Maintenance:** 20–80 mcg/kg/min by continuous infusion; **max. dose:** 2 g/24 hr**Adult:****IM:** 50 mg/kg/24 hr  $\div$  Q3–6 hr**IV: Loading:** 50–100 mg/dose. Repeat dose Q5 min PRN to a **max. total dose** of 1000–1500 mg.**Maintenance:** 1–6 mg/min by continuous infusion**NOTE:** IV infusion dosage units for adults are in mg/min, compared with mcg/kg/min for children.**Contraindicated** in myasthenia gravis, complete heart block, SLE, and torsades de pointes.**Use with caution** in asymptomatic PVCs, digitalis intoxication, CHF, renal or hepatic dysfunction. **Adjust dose in renal failure (see Chapter 31).**May cause lupus-like syndrome, positive Coombs test, thrombocytopenia, arrhythmias, GI complaints, and confusion. Increased LFTs and liver failure have been reported. Monitor BP and ECG when using IV. QRS widening by  $>0.02$  sec suggests toxicity.

PROCAINAMIDE *continued*

Do not use with desipramine and other TCAs. Cimetidine, ranitidine, amiodarone,  $\beta$ -blockers, and trimethoprim may increase procainamide levels. Procainamide may enhance effects of skeletal muscle relaxants and anticholinergic agents. Therapeutic levels: 4–10 mg/L of procainamide or 10–30 mg/L of procainamide and NAPA levels combined.

**Recommended serum sampling times:**

**IM intermittent dosing:** Trough level within 30 min before next scheduled dose after 2 days of continuous dosing (steady state).

**IV continuous infusion:** 2 and 12 hr after start of infusion and at 24-hr intervals thereafter.

**PROCHLORPERAZINE**

Compazine and generics

**Antiemetic, phenothiazine derivative**



No



No



2



?

**Tabs (as maleate):** 5, 10 mg

**Suppository:** 25 mg (12s)

**Injection (as edisylate):** 5 mg/mL (2, 10 mL); may contain bisulfites and benzyl alcohol

**Antiemetic doses:**

**Child (>10 kg or > 2 yr):**

**PO or PR:** 0.4 mg/kg/24 hr  $\div$  TID–QID **OR** alternative dosing by weight:

**10–14 kg:** 2.5 mg once daily–BID; **max. dose:** 7.5 mg/24 hr

**15–18 kg:** 2.5 mg BID–TID; **max. dose:** 10 mg/24 hr

**19–39 kg:** 2.5 mg TID or 5 mg BID; **max. dose:** 15 mg/24 hr

**>39 kg:** Use adult dose.

**IM:** 0.1–0.15 mg/kg/dose TID–QID; **max. dose:** 10 mg/single dose or 40 mg/24 hr

**Adult:**

**PO:** 5–10 mg/dose TID–QID; **max. dose:** 40 mg/24 hr

**PR:** 25 mg/dose BID

**IM:** 5–10 mg/dose Q3–4 hr

**IV:** 2.5–10 mg/dose; may repeat Q3–4 hr

**Max. IM/IV dose:** 40 mg/24 hr

**Psychoses:**

**Child 2–12 yr and >9 kg:**

**PO:** Start with 2.5 mg BID–TID with a **max. first day dose** of 10 mg/24 hr. Dose may be increased as needed to 20 mg/24 hr for children 2–5 yr and 25 mg/24 hr for 6–12 yr.

**IM:** 0.13 mg/kg/dose  $\times$  1 and convert to PO immediately.

**Adult:**

**PO:** 5–10 mg TID–QID; may be increased as needed to a **max. dose** of 150 mg/24 hr.

**IM:** 10–20 mg Q2–4 hr PRN; convert to PO immediately.

Toxicity as for other phenothiazines (see *Chlorpromazine*). Extrapyramidal reactions (reversed by diphenhydramine) or orthostatic hypotension may occur. May mask signs and symptoms of overdosage of other drugs and may obscure diagnosis and treatment of conditions such as intestinal obstruction, brain tumor, and Reye syndrome. May cause false-positive test for phenylketonuria, urinary amylase, uroporphyrins, and urobilinogen. **Do not use IV route** in children. Use only in management of prolonged vomiting of known etiology.

For children 5–18 yr, a 0.15-mg/kg/dose IV over 10 min was effective in migraine headaches presenting in emergency departments (see *Ann Emerg Med*. 2004;43:256–262).

**Pregnancy category has not been formally assigned by the FDA.**



**PROMETHAZINE**

Phenergan and generics

**Antihistamine, antiemetic, phenothiazine derivative**

No



No



3



C

**Tabs:** 12.5, 25, 50 mg**Oral solution/syrup:** 6.25 mg/5 mL (118, 473 mL); contains alcohol**Suppository:** 12.5, 25, 50 mg (12s)**Injection:** 25, 50 mg/mL (1 mL); may contain sulfites**Antihistaminic:****Child ≥ 2 yr:** 0.1 mg/kg/dose (**max. dose:** 12.5 mg/dose) Q6 hr PO during daytime hours and 0.5 mg/kg/dose (**max. dose:** 25 mg/dose) QHS PO PRN**Adult:** 6.25–12.5 mg PO/PR TID and 25 mg QHS**Nausea and vomiting PO/IM/IV/PR (see remarks):****Child ≥ 2 yr:** 0.25–1 mg/kg/dose Q4–6 hr PRN; **max. dose:** 25 mg/dose**Adult:** 12.5–25 mg Q4–6 hr PRN**Motion sickness: (1st dose 0.5–1 hr before departure):****Child ≥ 2 yr:** 0.5 mg/kg/dose Q12 hr PO/PR PRN; **max. dose:** 25 mg/dose**Adult:** 25 mg PO Q8–12 hr PRN

**Avoid** use in children <2 yr because of risk for fatal respiratory depression. Toxicity similar to other phenothiazines (see *Chlorpromazine*). **Do not** administer SC or intraarterially because of severe local reactions. IV route of administration is **not recommended** (IM preferred) owing to severe tissue injury (tissue necrosis and gangrene). If using IV route, dilute 25 mg/mL–strength product with 10–20 mL NS, and administer over 10–15 min; consider lower initial doses, administer through a large-bore vein, check patency of line before administering, administer through an IV line at the port farthest from the patient's vein, and monitor for burning or pain during or after injection. Administer oral doses with meals to decrease GI irritation.

May cause profound sedation, blurred vision, respiratory depression (use lowest effective dose in children and **avoid** concomitant use of respiratory depressants), and dystonic reactions (reversed by diphenhydramine). Cholestatic jaundice and neuroleptic malignant syndrome has been reported. May interfere with pregnancy tests (immunologic reactions between hCG and anti-hCG). **For nausea and vomiting, use only in management of prolonged vomiting of known etiology.**

**PROPRANOLOL**

Inderal, Inderal LA, and generics

**Adrenergic blocking agent (beta), class II antiarrhythmic**

Yes



Yes



1



C/D

**Tabs:** 10, 20, 40, 60, 80 mg**Extended-release caps (Inderal LA and others):** 60, 80, 120, 160 mg**Oral solution:** 20 mg/5 mL, 40 mg/5 mL; contains parabens and saccharin**Concentrated solution:** 80 mg/mL; alcohol and dye free**Injection:** 1 mg/mL (1 mL)**Arrhythmias:****Child:****IV:** 0.01–0.1 mg/kg/dose IV push over 10 min, repeat Q6–8 hr PRN; **max. dose:** 1 mg/dose for infant; 3 mg/dose for child**PO:** Start at 0.5–1 mg/kg/24 hr ÷ Q6–8 hr; increase dosage Q3–5 days PRN. Usual dosage range: 2–4 mg/kg/24 hr ÷ Q6–8 hr; **max. dose:** 60 mg/24 hr or 16 mg/kg/24 hr

PROPRANOLOL *continued***Adult:**

**IV:** 1 mg/dose Q5 min up to **total** 5 mg

**PO:** 10–20 mg/dose TID–QID; increase PRN. Usual range: 40–320 mg/24 hr ÷ TID–QID.

**Hypertension:****Child:**

**PO:** Initial: 0.5–1 mg/kg/24 hr ÷ Q6–12 hr. May increase dose Q5–7 days PRN to **max. dose** of 8 mg/kg/24 hr.

**Adult:**

**PO:** 40 mg/dose PO BID or 60–80 mg/dose (sustained-release capsule) PO once daily. May increase 10–20 mg/dose Q3–7 days; **max. dose:** 640 mg/24 hr

**Migraine prophylaxis:****Child:**

**<35 kg:** 10–20 mg PO TID

**≥35 kg:** 20–40 mg PO TID

**Adult:** 80 mg/24 hr ÷ Q6–8 hr PO; increase dose by 20–40 mg/dose Q3–4 wk PRN. Usual effective dose range: 160–240 mg/24 hr.

**Tetralogy spells:**

**IV:** 0.15–0.25 mg/kg/dose slow IV push. May repeat in 15 min × 1. See Chapter 7.

**PO:** Start at 2–4 mg/kg/24 hr ÷ Q6 hr PRN. Usual dose range: 4–8 mg/kg/24 hr ÷ Q6 hr PRN. Doses as high as 15 mg/kg/24 hr have been used with careful monitoring.

**Thyrototoxicosis:**

**Neonate:** 2 mg/kg/24 hr PO ÷ Q6–12 hr

**Adolescent and adult:**

**IV:** 1–3 mg/dose over 10 min. May repeat in 4–6 hr.

**PO:** 10–40 mg/dose PO Q6 hr

**Infantile hemangioma (see remarks):**

Start at 1 mg/kg/24 hr ÷ Q8 hr PO. If tolerated after 1 day, increase dose to 2 mg/kg/24 hr ÷ Q8 hr PO.

**Contraindicated** in asthma, Raynaud syndrome, heart failure, and heart block. **Not indicated** for treatment of hypertensive emergencies. **Use with caution** in presence of obstructive lung disease, diabetes mellitus, renal or hepatic disease. May cause hypoglycemia, hypotension, nausea, vomiting, depression, weakness, impotence, bronchospasm, and heart block. Cutaneous reactions, including Stevens-Johnson syndrome, TEN, exfoliative dermatitis, erythema multiforme, and urticaria have been reported. Acute hypertension has occurred after insulin-induced hypoglycemia in patients on propranolol.

**Therapeutic levels:** 30–100 ng/mL. Drug is metabolized by CYP 450 1A2, 2C18, 2C19, and 2D6 isoenzymes. Concurrent administration with barbiturates, indomethacin, or rifampin may cause decreased activity of propranolol. Concurrent administration with cimetidine, hydralazine, flecainide, quinidine, chlorpromazine, or verapamil may lead to increased activity of propranolol. **Avoid** IV use of propranolol with calcium channel blockers; may increase effect of calcium channel blocker. Use with amiodarone may increase negative chronotropic effects.

For infantile hemangioma, monitor BP, HR, and blood glucose. Infants <6 mo must be fed Q4 hr.

Successful use in infantile hepatic hemangiomas has also been reported.

Pregnancy category changes to "D" if used in second or third trimesters.





**PROPYLTHIOURACIL**

PTU and generics

**Antithyroid agent**

Yes



Yes



2



D

**Tabs:** 50 mg**Oral suspension:** 5 mg/mL 

100 mg PTU = 10 mg methimazole

Dosages should be adjusted as required to achieve and maintain  $T_4$ , TSH levels in normal ranges.

**Neonate:** 5–10 mg/kg/24 hr ÷ Q8 hr PO**Child:****Initial:** 5–7 mg/kg/24 hr ÷ Q8 hr PO, OR by age:**6–10 yr:** 50–150 mg/24 hr ÷ Q8 hr PO**>10 yr:** 150–300 mg/24 hr ÷ Q8 hr PO**Maintenance:** Generally begins after 2 mo. Usually  $\frac{1}{3}$ – $\frac{2}{3}$  initial dose in divided doses (Q8–12 hr) when patient is euthyroid.**Adult:****Initial:** 300–400 mg/24 hr ÷ Q6–8 hr PO; some may require larger doses of 600–900 mg/24 hr.**Maintenance:** 100–150 mg/24 hr ÷ Q8 hr PO

May cause blood dyscrasias, fever, liver disease, dermatitis, urticaria, malaise, CNS stimulation or depression, and arthralgias. Glomerulonephritis, severe liver injury/failure, agranulocytosis, interstitial pneumonitis, exfoliative dermatitis, and erythema nodosum have also been reported. May decrease effectiveness of warfarin. Monitor thyroid function. A dose reduction of  $\beta$ -blocker may be necessary when hyperthyroid patient becomes euthyroid.



For neonates, crush tablets, weigh appropriate dose, and mix in formula/breast milk. **Adjust dose in renal failure (see Chapter 31).**

**PROSTAGLANDIN  $E_1$** 

See Alprostadil

**PROTAMINE SULFATE**

Various generic brands

**Antidote, heparin**

No



No



?



C

**Injection:** 10 mg/mL (5, 25 mL); preservative free**Heparin antidote, IV:**

1 mg protamine will neutralize 115 U porcine intestinal heparin, 90 U beef lung heparin, or 100 U (1 mg) low-molecular-weight heparin.

**Consider time since last heparin dose:****If < 0.5 hr:** Give 100% of specified dose.**If within 0.5–1 hr:** Give 50%–75% of aforementioned dose.**If within 1–2 hr:** Give 37.5%–50% of aforementioned dose.**If  $\geq$  2 hr:** Give 25%–37.5% of aforementioned dose.**Max. dose:** 50 mg IV**Max. infusion rate:** 5 mg/min**Max. IV concentration:** 10 mg/mL

PROTAMINE SULFATE *continued*

**If heparin was administered by deep SC injection, give 1–1.5 mg protamine per 100 U heparin as follows:**

Load with 25–50 mg via slow IV infusion, followed by rest of calculated dose via continuous infusion over 8–16 hr or expected duration of heparin absorption.

**Enoxaparin overdosage, IV (see remarks):**  $\approx$  1 mg protamine will neutralize 1 mg enoxaparin.

**Consider time since last enoxaparin dose:**

**If < 8 hr:** Give 100% of aforementioned dose.

**If within 8–12 hr:** Give 50% of aforementioned dose.

**If > 12 hr:** Protamine not required, but if serious bleeding is present, give 50% of aforementioned dose.

If APTT remains prolonged 2–4 hr after first protamine dose, a second infusion of 0.5 mg protamine per 1 mg enoxaparin may be given.

**Max. dose:** 50 mg. See *Heparin* antidote IV dosage for **max.** administration concentration and rate.

Risk factors for protamine hypersensitivity include known hypersensitivity to fish and exposure to protamine-containing insulin or prior protamine therapy.

May cause hypotension, bradycardia, dyspnea, and anaphylaxis. Monitor APTT or ACT.

Heparin rebound with bleeding has been reported to occur 8–18 hr later.

Use in enoxaparin overdose may not be complete despite using multiple doses of protamine.



## PSEUDOEPHEDRINE

Sudafed, Sudafed 12 Hour, Sudafed 24 Hour, and generics

**Sympathomimetic, nasal decongestant**



No



Yes



2



C

**Tabs [OTC]:** 30, 60 mg

**Extended-release tab [OTC]:**

**Sudafed 12 Hour:** 120 mg

**Sudafed 24 Hour:** 240 mg

**Oral liquid [OTC]:** 15 mg/5 mL, 30 mg/5 mL (120, 473 mL)

**Oral syrup [OTC]:** 30 mg/5 mL (473 mL); contains parabens

**Purchases of OTC products are limited to behind the pharmacy counter sales, with monthly sale limits because of the methamphetamine epidemic.**

**Child < 12 yr:** 4 mg/kg/24 hr  $\div$  Q6 hr PO or by age:

**<4 yr:** 4 mg/kg/24 hr  $\div$  Q6 hr PO

**4–5 yr:** 15 mg/dose Q4–6 hr PO; **max. dose:** 60 mg/24 hr

**6–12 yr:** 30 mg/dose Q4–6 hr PO; **max. dose:** 120 mg/24 hr

**Child  $\geq$  12 yr and adult:**

**Immediate release:** 30–60 mg/dose Q4–6 hr PO; **max. dose:** 240 mg/24 hr

**Sustained release:**

**Sudafed 12 Hour:** 120 mg PO Q12 hr

**Sudafed 24 Hour:** 240 mg PO Q24 hr



**Contraindicated** with MAOI drugs and in severe hypertension and severe coronary artery disease. **Use with caution** in mild/moderate hypertension, hyperglycemia, hyperthyroidism, and cardiac disease. May cause dizziness, nervousness, restlessness, insomnia, and arrhythmias. Pseudoephedrine is a common component of OTC cough and cold preparations and is combined with several antihistamines; these products are not recommended for children <6 yr. Because drug and active metabolite are primarily excreted renally, **doses should be adjusted in renal impairment.** May cause false-positive test for amphetamines (EMIT assay).



**PSYLLIUM**

Metamucil, Fiberall, Konsyl, Reguloid, and many others

**Bulk-forming laxative**

No



No



1



B

**Granules [OTC]:** 100% psyllium (Konsyl: 6 g/rounded teaspoon) (300 g); contains maltodextrin; sugar and gluten free

**Powder [OTC]:** 100% psyllium, some versions containing sucrose (sugar-free version available) (Metamucil: 3.4 g/rounded teaspoon). For other products, check label for amount of psyllium per unit of measurement.

**Caps (Konsyl and Reguloid):** 0.52 g

3.4 g psyllium hydrophilic mucilloid is equivalent to 2 g soluble fiber.

**Constipation (granules or powder must be mixed with a full glass of water or juice):**

**<6 yr:** 1.25–2.5 g/dose PO once daily–TID; **max. dose:** 7.5 g/24 hr

**6–11 yr:** 2.5–3.75 g/dose PO once daily–TID; **max. dose:** 15 g/24 hr

**≥12 yr and adult:** 2.5–7.5 g/dose PO once daily–TID; **max. dose:** 30 g/24 hr



**Contraindicated** in cases of fecal impaction or GI obstruction. **Use with caution** in patients with esophageal strictures and rectal bleeding. Phenylketonurics should be aware that certain preparations may contain aspartame. Should be taken with a full glass (240 mL) of liquid. Onset of action: 12–72 hr.

**PYRANTEL PAMOATE**

Reese's Pinworm, Pamix, Pin-Rid, Pin-X, and generics

**Anthelmintic**

Yes



No



?



C

**Oral suspension [OTC]:** 50 mg/mL pyrantel base (144 mg/mL pyrantel pamoate) (30, 60, 240 mL); may contain sodium benzoate, parabens, and saccharin

**Tabs [OTC]:** 62.5 mg pyrantel base (180 mg pyrantel pamoate)

**Chewable tabs [OTC]:** 250 mg pyrantel base (720.5 mg pyrantel pamoate); contains aspartame

**All doses expressed in terms of pyrantel base.**

**Child (≥2 yr) and adult:**



**Ascaris (roundworm) and Trichostrongylus:** 11 mg/kg/dose PO × 1

**Enterobius (pinworm):** 11 mg/kg/dose PO × 1. Repeat same dose 2 wk later.

**Hookworm or eosinophilic enterocolitis:** 11 mg/kg/dose PO once daily × 3 days

**Moniliformis:** 11 mg/kg/dose PO × 1. Repeat twice 2 weeks apart.

**Max. dose (all indications):** 1 g/dose

**Use with caution** in liver dysfunction. **Do not use** in combination with piperazine because of antagonism. May cause nausea, vomiting, anorexia, transient AST elevations, headaches, rash, and muscle weakness. Limited experience in children <2 yr. May increase theophylline levels. Drug may be mixed with milk or fruit juice and may be taken with food.



**PYRAZINAMIDE**

Pyrazinoic acid amide and generics

**Antituberculous agent**

Yes



Yes



2



C

**Tab:** 500 mg**Oral suspension:** 10, 100 mg/mL **In combination with isoniazid and rifampin (Rifater):****Tab:** 300 mg with 50 mg isoniazid and 120 mg rifampin; contains povidone and propylene glycol**Tuberculosis:** Use as part of a multidrug regimen for tuberculosis. See latest edition of AAP *Red Book* for recommended treatment for tuberculosis.**Child:****Daily dose:** 30–40 mg/kg/24 hr PO ÷ once daily–BID; **max. dose:** 2 g/24 hr**Twice-weekly dose:** 50 mg/kg/dose PO 2 × per week; **max. dose:** 2 g/dose**Adult:****Daily dose:** 15–30 mg/kg/24 hr PO ÷ once daily–QID; **max. dose:** 2 g/24 hr**Twice-weekly dose:** 50–70 mg/kg/dose PO 2 × per week; **max. dose:** 4 g/dose**Mycobacterium tuberculosis in HIV, prophylaxis to prevent first episode:****Infant and child:** Not recommended because of increased risk of severe/fatal hepatotoxicity**Adolescent and adult:** 15–20 mg/kg/24 hr PO once daily × 2 mo in combination with either 600 mg rifampin PO once daily × 2 mo or 300 mg rifabutin PO once daily × 2 moSee latest edition of the AAP *Red Book* for recommended treatment for tuberculosis.**Contraindicated** in severe hepatic damage and acute gout. The CDC and ATS **do not recommend** the combination of pyrazinamide and rifampin for latent TB infections. **Use with caution** in patients with renal failure (dosage reduction has been recommended), gout, or diabetes mellitus. Monitor liver function tests (baseline and periodic) and serum uric acid.

Hepatotoxicity is most common dose-related side effect; doses ≤30 mg/kg/24 hr minimize effect.

Hyperuricemia, maculopapular rash, arthralgia, fever, acne, porphyria, dysuria, and photosensitivity may occur. Severe hepatic toxicity may occur with rifampin use. May decrease isoniazid levels.

**PYRETHRINS WITH PIPERONYL BUTOXIDE**

Tisit, A-200, Pyriny, Pronto, RID, Licide, Klout, and others

**Pediculicide**

No



No



2



C

**All products are available without a prescription.****Lotion (Tisit):** 0.3% pyrethrins and 2% piperonyl butoxide (59, 118 mL); contains petroleum distillate and equivalent to 1.6% ether**Gel (Tisit):** 0.3% pyrethrins and 3% piperonyl butoxide (30 mL)**Shampoo (Tisit, RID, Pronto, Licide, Klout, A-200):** 0.33% pyrethrins and 4% piperonyl butoxide (60, 120, 240 mL); may contain alcohol**Mousse (RID):** 0.33% pyrethrins and 4% piperonyl butoxide (165 mL); contains alcohol**Pediculosis:** Apply to hair or affected body area for 10 min, then wash thoroughly and comb with fine-tooth or nit-removing comb; repeat in 7–10 days.**Contraindicated** in ragweed hypersensitivity; drug is derived from chrysanthemum flowers. For topical use only. **Avoid** use in and around the eyes, mouth, nose, or vagina. **Avoid** repeat applications in <24 hr. Low ovicidal activity requires repeat treatment. Dead nits require mechanical removal. Wash bedding and clothing to eradicate infestation.

Local irritation, including erythema, pruritus, urticaria, edema, and eczema may occur.

**PYRIDOSTIGMINE BROMIDE**

Mestinon, Regonol, and generics

**Cholinergic agent**

No



Yes



1



B

**Oral syrup:** 60 mg/5 mL (480 mL); contains 5% alcohol**Tabs:** 60 mg**Sustained-release tab:** 180 mg**Injection (Regonol):** 5 mg/mL (2 mL); may contain 0.2% parabens and benzyl alcohol**Myasthenia gravis:****Neonate:****PO:** 5 mg/dose Q4–6 hr**IM/IV:** 0.05–0.15 mg/kg/dose Q4–6 hr; **max. single IM/IV dose:** 10 mg**Child:****PO:** 7 mg/kg/24 hr in 5–6 divided doses**IM/IV:** 0.05–0.15 mg/kg/dose Q4–6 hr; **max. single IM/IV dose:** 10 mg**Adult:****PO (immediate release):** 60 mg TID; increase Q48 hr PRN. Usual effective dose: 60–1500 mg/24 hr.**PO (sustained release):** 180–540 mg once daily–BID**IM/IV (use when PO therapy is not practical):** Give 1/30 of the usual PO.

**Contraindicated** in mechanical intestinal or urinary obstruction. **Use with caution** in patients with epilepsy, asthma, bradycardia, hyperthyroidism, arrhythmias, or peptic ulcer. May cause nausea, vomiting, diarrhea, rash, headache, and muscle cramps. Pyridostigmine is mainly excreted unchanged by the kidney. Therefore, lower doses titrated to effect in renal disease may be necessary.

Changes in oral dosages may take several days to show results. **Atropine is the antidote.**

**PYRIDOXINE**Vitamin B<sub>6</sub>, and various names, including generics**Vitamin, water soluble**

No



No



1



A/C

**Tabs (HCl) [OTC]:** 25, 50, 100, 250, 500 mg**Oral solution (HCl):** 1 mg/mL **Injection (HCl):** 100 mg/mL (1 mL); some products may contain aluminum.**Deficiency, IM/IV/PO (PO preferred):**

**Child:** 5–25 mg/24 hr × 3 wk, followed by 2.5–5 mg/24 hr as maintenance therapy (via multivitamin preparation)

**Adolescent and adult:** 10–20 mg/24 hr × 3 wk, followed by 2–5 mg/24 hr as maintenance therapy (via multivitamin preparation)

**Drug-induced neuritis (PO):****Prophylaxis:****Child:** 1 mg/kg/24 hr or 10–50 mg/24 hr**Adolescent and adult:** 25–50 mg/24 hr**Treatment (optimal dose not established):****Child:** 50–200 mg/24 hr**Adolescent and adult:** 50–300 mg/24 hr

PYRIDOXINE *continued***Pyridoxine-dependent seizures:****Neonate and infant:****Initial:** 50–100 mg/dose IM or rapid IV  $\times$  1**Maintenance:** 50–100 mg/24 hr PO**Recommended daily allowance:** See Chapter 21.

**Use caution** with concurrent levodopa therapy. Chronic administration has been associated with sensory neuropathy. Nausea, headache, increased AST, decreased serum folic acid level, and allergic reaction may occur. May lower phenobarbital and phenytoin levels. See Chapter 20 for management of neonatal seizures.

Pregnancy category changes to "C" if dosage exceeds U.S. RDA recommendation.

**PYRIMETHAMINE**

Daraprim

**Antiparasitic agent**

Yes



Yes



2



C

**Tabs:** 25 mg**Oral suspension:** 2 mg/mL 

Combination product with sulfadoxine (Fansidar) is no longer available in the United States.

**Congenital toxoplasmosis (administer with sulfadiazine and leucovorin [see remarks]):****Loading dose:** 2 mg/kg/24 hr PO  $\div$  Q12 hr  $\times$  2 days**Maintenance:** 1 mg/kg/24 hr PO once daily  $\times$  2–6 mo, then 1 mg/kg/24 hr 3  $\times$  per wk to complete total 12 mo of therapy**Toxoplasmosis (administer with sulfadiazine or trisulfapyrimidines, and leucovorin):****Child:****Loading:** 2 mg/kg/24 hr PO  $\div$  BID  $\times$  3 days; **max. dose:** 100 mg/24 hr**Maintenance:** 1 mg/kg/24 hr PO  $\div$  once daily–BID  $\times$  4 wk; **max. dose:** 25 mg/24 hr**Adult:** 50–75 mg/24 hr  $\times$  3–4 wk depending on response. After response, decrease dose by 50% and continue for an additional 4–5 wk.

Pyrimethamine is a folate antagonist. Supplementation with folic acid leucovorin at 5–15 mg/24 hr is recommended. **Contraindicated** in megaloblastic anemia secondary to folate deficiency. **Use with caution** in G6PD deficiency, malabsorption syndromes, alcoholism, pregnancy, and renal or hepatic impairment. Pyrimethamine can cause glossitis, bone marrow suppression, seizures, rash, and photosensitivity. For congenital toxoplasmosis, see *Clin Infect Dis*. 1994;18:38–72. Zidovudine and methotrexate may increase risk for bone marrow suppression. Aurothioglucose, trimethoprim, and sulfamethoxazole may increase risk for blood dyscrasias. Administer doses with meals. Most cases of acquired toxoplasmosis **do not** require specific antimicrobial therapy.

**QUINIDINE**

Various generic brands

**Class Ia antiarrhythmic**

Yes



Yes



2




C

**As gluconate (62% quinidine):****Slow-release tabs:** 324 mg**Injection:** 80 mg/mL (50 mg/mL quinidine) (10 mL); contains phenol**As sulfate (83% quinidine):***Continued*

QUINIDINE *continued*

**Tabs:** 200, 300 mg

**Slow-release tab:** 300 mg

**Oral suspension:** 10 mg/mL 

Equivalents: 200 mg sulfate = 267 mg gluconate

All doses expressed as salt forms.

**Antiarrhythmic:**

**Child (give PO as sulfate; give IM/IV as gluconate):**

**Test dose:** 2 mg/kg  $\times$  1 IM/PO; **max. dose:** 200 mg

**Therapeutic dose:**

**IV (as gluconate):** 2–10 mg/kg/dose Q3–6 hr PRN

**PO (as sulfate):** 15–60 mg/kg/24 hr  $\div$  Q6 hr

**Adult (give PO as sulfate; give IM as gluconate):**

**Test dose:** 200 mg  $\times$  1 IM/PO

**Therapeutic dose:**

**As sulfate:**

**PO, immediate-release:** 100–600 mg/dose Q4–6 hr. Begin at 200 mg/dose and titrate to desired effect.

**PO, sustained release:** 300–600 mg/dose Q 8–12 hr

**As gluconate:**

**IM:** 400 mg/dose Q4–6 hr

**IV:** 200–400 mg/dose, infused at a rate of  $\leq 10$  mg/min

**PO:** 324–972 mg Q8–12 hr

**Malaria:**

**Child and adult (give IV as gluconate [see remarks]):**

**Loading dose:** 10 mg/kg/dose (**max. dose:** 600 mg) IV over 1–2 hr, followed by maintenance dose. Omit or decrease load if patient has received quinine or mefloquine.

**Maintenance dose:** 0.02 mg/kg/min IV as continuous infusion until oral therapy can be initiated. If more than 48 hr of IV therapy is required, reduce dose by 30%–50%.

Test dose is given to assess for idiosyncratic reaction to quinidine. Toxicity indicated by increase of QRS interval by  $\geq 0.02$  sec (skip dose or stop drug). May cause GI symptoms, hypotension, tinnitus, TTP, rash, heart block, and blood dyscrasias. When used alone, may cause 1:1 conduction in atrial flutter, leading to ventricular fibrillation. May get idiosyncratic ventricular tachycardia with low levels, especially when initiating therapy.



Quinidine is a substrate of CYP 450 3A3/4 and 3A5–7 enzymes, and an inhibitor of CYP 450 2D6 and 3A3/4 enzymes. Can cause increase in digoxin levels. Quinidine potentiates effect of neuromuscular blocking agents,  $\beta$ -blockers, anticholinergics, and warfarin. Amiodarone, antacids, delavirdine, diltiazem, grapefruit juice, saquinavir, ritonavir, verapamil, or cimetidine may enhance drug's effect. Barbiturates, phenytoin, cholinergic drugs, nifedipine, sucralfate, or rifampin may reduce quinidine's effect. **Use with caution** in renal insufficiency (15%–25% of drug is eliminated unchanged in the urine), myocardial depression, sick sinus syndrome, G6PD deficiency, and hepatic dysfunction.

**Therapeutic levels:** 3–7 mg/L. Recommended serum sampling times at steady state: trough level obtained within 30 min before next scheduled dose after 1–2 days of continuous dosing (steady state).

**MALARIA USE:** Continuous monitoring of ECG, BP, and serum glucose are recommended, especially in pregnant women and young children.

**QUINUPRISTIN AND DALFOPRISTIN**

Synercid

**Antibiotic, streptogramin**

Yes



No



?



B

**Injection:** 500 mg (150 mg quinupristin and 350 mg dalfopristin)**Doses expressed in mg of combined quinupristin and dalfopristin.****Vancomycin-resistant *Enterococcus faecium* (VREF):****Child < 16 yr (limited data), ≥ 16 yr and adult:** 7.5 mg/kg/dose IV Q8 hr**Complicated skin infections:****Child < 16 yr (limited data), ≥ 16 yr and adult:** 7.5 mg/kg/dose IV Q12 hr for at least 7 days**VREF endocarditis:****Child and adult:** 7.5 mg/kg/dose IV Q8 hr for at least 8 weeks

**Not active** against *Enterococcus faecalis*. **Use with caution** in hepatic impairment; dosage reduction may be necessary. Most common side effects include pain, burning, inflammation and edema at IV infusion site, thrombophlebitis and thrombosis, GI disturbances, rash, arthralgia, myalgia, increased liver enzymes, hyperbilirubinemia, and headache. Dose-frequency reductions (Q8 hr to Q12 hr) or discontinuation can improve severe cases of arthralgia and myalgia. Use total body weight for obese patients when calculating dosages.

Drug is an inhibitor of CYP 450 3A4 isoenzyme. **Avoid use** with CYP 450 3A4 substrates, which can prolong QTc interval (e.g., cisapride). May increase effects/toxicity of cyclosporine, tacrolimus, sirolimus, delavirdine, nevirapine, indinavir, ritonavir, diazepam, midazolam, carbamazepine, methylprednisolone, vinca alkaloids, docetaxel, paclitaxel, quinidine, and some calcium channel blockers.

**Pediatric pharmacokinetic studies have not been completed.** Reduce dose for patients with hepatic cirrhosis (Child-Pugh A or B).

Drug is compatible with D<sub>5</sub>W and incompatible with saline and heparin. Infuse each dose over 1 hr using the following **max. IV concentrations:** peripheral line, 2 mg/mL; central line, 5 mg/mL. If injection site reaction occurs, dilute infusion to <1 mg/mL.

**RANITIDINE HCL**

Zantac, Zantac 75 [OTC], Zantac 150 Maximum Strength [OTC], and many generics

**Histamine-2-antagonist**

Yes



Yes



1



B

**Tabs:** 75 [OTC], 150 [OTC and Rx], 300 mg**Caps:** 150, 300 mg**Oral syrup:** 15 mg/mL (480 mL); may contain 7.5% alcohol and parabens**Injection:** 25 mg/mL (2, 6, 40 mL); may contain 0.5% phenol**Neonate:****PO:** 2–4 mg/kg/24 hr ÷ Q8–12 hr**IV:** 2 mg/kg/24 hr ÷ Q6–8 hr**≥1 mo–16 yr:****Duodenal/gastric ulcer (see remarks):****PO:****Treatment:** 4–8 mg/kg/24 hr ÷ Q12 hr; **max. dose:** 300 mg/24 hr**Maintenance:** 2–4 mg/kg/24 hr ÷ Q12 hr; **max. dose:** 150 mg/24 hr**IV/IM:** 2–4 mg/kg/24 hr ÷ Q6–8 hr; **max. dose:** 200 mg/24 hr

Continued



RANITIDINE HCL *continued***GERD/erosive esophagitis:**

**PO:** 5–10 mg/kg/24 hr ÷ Q8–12 hr. **GERD max. dose:** 300 mg/24 hr; **erosive esophagitis max. dose:** 600 mg/24 hr

**IV/IM:** 2–4 mg/kg/24 hr ÷ Q6–8 hr; **max. dose:** 200 mg/24 hr

**Adolescent and adult:**

**PO:** 150 mg/dose BID or 300 mg/dose QHS

**IM/IV:** 50 mg/dose Q6–8 hr; **max. dose:** 400 mg/24 hr

**Continuous infusion, all ages:** Administer daily IV dosage over 24 hr (may be added to parenteral nutrition solutions).

May cause headache and GI disturbance, malaise, insomnia, sedation, arthralgia, and hepatotoxicity. May increase levels of nifedipine and midazolam. May decrease levels of ketoconazole, itraconazole, and delavirdine. May cause false-positive urine protein test (Multistix).

Duodenal/gastric ulcer doses for ≥1 mo–16 yr are extrapolated from clinical adult trials and pharmacokinetic data in children. Extemporaneously compounded carbohydrate-free oral solution dosage form is useful for patients receiving the ketogenic diet. The syrup dosage form has a peppermint flavor and may not be tolerated. **Adjust dose in renal failure (see Chapter 31).**

**RASBURICASE**

Elitek

**Antihyperuricemic agent**



No



No



?



C

**Injection:** 1.5, 7.5 mg; contains mannitol

**Hyperuricemia:** 0.1–0.2 mg/kg/dose (rounded down to nearest whole 1.5 mg multiple) IV over 30 min × 1. Patients generally respond to 1 dose, but if needed, dose may be repeated Q24 hr for up to 4 additional doses.



**Contraindicated** in G6PD deficiency or history of hypersensitivity, hemolytic reactions, or methemoglobinemia with rasburicase. **Use with caution** in asthma, allergies, hypersensitivity with other medications, and children <2 yr (decreased efficacy and increased risk for rash, vomiting, diarrhea, and fever).



Common side effects include nausea, vomiting, abdominal pain, discomfort, diarrhea, constipation, mucositis, fever, and rash.

During therapy, uric acid blood samples must be sent to the laboratory immediately. Blood should be collected in prechilled tubes containing heparin, and placed in an ice-water bath to avoid potential falsely low uric acid levels (degradation of plasma uric acid occurs in the presence of rasburicase at room temperature). Centrifugation in a precooled centrifuge (4°C) is indicated. Plasma samples must be assayed within 4 hr of sample collection.

**Rh<sub>0</sub>(D) IMMUNE GLOBULIN INTRAVENOUS (HUMAN)**

WinRho-SDF

*Immune globulin*

No



No



1



C

**Injection:** 1500 (1.3 mL), 2500 (2.2 mL), 5000 (4.4 mL), 15,000 IU (13 mL)**Conversion:** 1 mcg = 5 IU**All doses based on international units (IU).*****Immune thrombocytopenic purpura (nonsplenectomized Rh<sub>0</sub>(D)-positive patients):******Initial dose (may be given in two divided doses on separate days or as a single dose):******Hemoglobin  $\geq$  10 mg/dL:*** 250 IU/kg/dose IV  $\times$  1***Hemoglobin < 10 mg/dL:*** 125–200 IU/kg/dose IV  $\times$  1. See remarks for hemoglobin < 8 mg/dL.***Additional doses:******Responders to initial dose:*** 125–300 IU/kg/dose IV; actual dose and frequency of administration is determined by patient's response and subsequent hemoglobin level.***Non-responders to initial dose:******Hemoglobin < 8 g/dL:*** Alternative therapy should be used.***Hemoglobin 8–10 g/dL:*** 125–200 IU/kg/dose IV  $\times$  1***Hemoglobin > 10 g/dL:*** 250–300 IU/kg/dose  $\times$  1WinRho SDF is currently the only Rh<sub>0</sub>(D) immune globulin product indicated for ITP.

**Contraindicated** in IgA deficiency. **Use with extreme caution** in patients with a hemoglobin < 8 mg/dL and thrombocytopenia or bleeding disorders. Adverse events associated with ITP include headache, chills, fever, and reduction in hemoglobin (due to destruction of Rh<sub>0</sub>(D) antigen-positive red cells). Intravascular hemolysis resulting in anemia and renal insufficiency has been reported. May interfere with immune response to live virus vaccines (e.g., MMR, varicella). Rh<sub>0</sub>(D)-positive patients should be monitored for signs and symptoms of intravascular hemolysis, anemia, and renal insufficiency. Administer IV doses over 3–5 min.

**RIBAVIRIN**

Oral: Rebetol, Copegus, Ribasphere, and other generics

Inhalation: Virazole

**Antiviral agent**

Yes



Yes



?



X

**Oral solution (Rebetol):** 200 mg/5 mL (100 mL); contains sodium benzoate**Oral caps (Rebetol, Ribasphere):** 200 mg**Tabs:****Copegus:** 200 mg**Ribasphere:** 200, 400, 600 mg**Aerosol (Virazole):** 6 g**Hepatitis C (P0, see remarks):**

**Child  $\geq$  3 yr (in combination with interferon alfa-2b at 3 million units 3  $\times$  per wk SC; use oral solution or capsule):** 15 mg/kg/24 hr  $\div$  BID or by the following weight categories:

**25–36 kg:** 200 mg BID**37–49 kg:** 200 mg QAM and 400 mg QPM**50–61 kg:** 400 mg BID**>61–75 kg:** 400 mg QAM and 600 mg QPM**>75 kg:** 600 mg BID

Continued

RIBAVIRIN *continued***Duration of therapy:**

**Genotype 1:** 48 weeks. Consider discontinuing at 12 weeks if a 2-log decrease in viral load is achieved or if virus is still detectable at 24 weeks.

**Genotypes 2 and 3:** 24 weeks

**Dosage modification for toxicity:** See remarks.

**Adult:**

**Oral capsules in combination with interferon alfa-2b at 3 million units 3 × per week SC:**

≤75 kg: 400 mg QAM and 600 mg QPM

>75 kg: 600 mg BID

**Oral capsules in combination with peginterferon alfa-2b:** 400 mg BID

**Oral tablets in combination with peginterferon alfa-2a for hepatitis C genotype 1, 4:**

≤75 kg: 500 mg BID × 48 wk

>75 kg: 600 mg BID × 48 wk

**Oral tablets in combination with peginterferon alfa-2a for genotype 2, 3:** 400 mg BID × 24 wk

**Oral tablets in combination with peginterferon alfa-2a for HIV co-infected patient (regardless of hepatitis C genotype):** 400 mg BID × 48 wk

**Dosage modification for toxicity:** See remarks.

**Inhalation:**

**Continuous:** Administer 6 g by aerosol over 12–18 hr once daily for 3–7 days. The 6-g ribavirin vial is diluted in 300 mL preservative-free sterile water to a final concentration of 20 mg/mL. Must be administered with Viratek Small Particle Aerosol Generator (SPAG-2).

**Intermittent (for nonventilated patients):** Administer 2 g by aerosol over 2 hr TID for 3–7 days. The 6-g ribavirin vial is diluted in 100 mL preservative-free sterile water to a final concentration of 60 mg/mL. Intermittent use is not recommended in patients with endotracheal tubes.

**ORAL RIBAVIRIN:** Contraindicated in pregnancy, significant or unstable cardiac disease, autoimmune hepatitis, hepatic decompensation (Child-Pugh score > 6; class B or C), hemoglobinopathies, and creatinine clearance < 50 mL/min. **Use with caution** in preexisting cardiac disease, pulmonary disease, and sarcoidosis. Anemia (most common), insomnia, depression, irritability, and suicidal behavior (higher in adolescent and pediatric patients) have been reported with the oral route.



Tinnitus, hearing loss, vertigo, and severe hypertriglyceridemia have been reported in combination with interferon. Pancytopenia has been reported in combination with interferon and azathioprine.

Increased risk for hepatic decompensation with cirrhotic chronic hepatitis C patients treated with alpha interferons or with HIV co-infection receiving HAART and interferon alfa-2a.

May decrease effects of zidovudine, stavudine; and increase risk for lactic acidosis with nucleoside analogs. **Reduce or discontinue dosage for toxicity as follows:**

Patient with no cardiac disease:

**Hgb < 10 g/dL and ≥ 8.5 g/dL:**

**Child:** 12 mg/kg/dose PO once daily; may further reduce to 8 mg/kg/dose PO once daily

**Adult:** 600 mg PO once daily (capsules or solution) or 200 mg PO QAM and 400 mg PO QPM (tablets)

**Hgb < 8.5 g/dL:** Discontinue therapy permanently.

Patient with cardiac disease:

≥2 mg/dL decrease in Hgb during any 4-wk period during therapy:

**Child:** 12 mg/kg/dose PO once daily; may further reduce to 8 mg/kg/dose PO once daily (monitor weekly)

**Adult:** 600 mg PO once daily (capsules or solution) or 200 mg PO QAM and 400 mg PO QPM (tablets)

**Hgb < 12 g/dL after 4 wk of reduced dose:** Discontinue therapy permanently.

RIBAVIRIN *continued*

**INHALED RIBAVIRIN:** Use of ribavirin for RSV is controversial and **not** routinely indicated. Aerosol therapy may be considered for selected infants and young children at high risk for serious RSV disease (see most recent edition of *AAP Red Book*). Most effective if begun early in course of RSV infection, generally in first 3 days. May cause worsening respiratory distress, rash, conjunctivitis, mild bronchospasm, hypotension, anemia, and cardiac arrest. **Avoid** unnecessary occupational exposure to ribavirin owing to its teratogenic effects. Drug can precipitate in respiratory equipment.

**RIBOFLAVIN**Vitamin B<sub>2</sub> and various brands and generics**Water-soluble vitamin**

No



No



1



A/C

**Tabs [OTC]:** 25, 50, 100 mg**Caps [OTC]:** 50, 400 mg**Riboflavin deficiency:****Child:** 2.5–10 mg/24 hr ÷ once daily–BID PO**Adult:** 5–30 mg/24 hr ÷ once daily–BID PO**U.S. RDA requirements:** *see Chapter 21.*

Hypersensitivity may occur. Administer with food. Causes yellow to orange discoloration of urine. For multivitamin information, see Chapter 21.



Pregnancy category changes to "C" if used in doses above the RDA.

**RIFABUTIN**

Mycobutin

**Antituberculous agent**

Yes




Yes



3



B

**Caps:** 150 mg**Oral suspension:** 20 mg/mL 

**MAC prophylaxis for first episode and recurrence of opportunistic disease in HIV (see remarks for interactions and [www.aidsinfo.nih.gov/guidelines](http://www.aidsinfo.nih.gov/guidelines)):**



**≥6 yr and adult:** 300 mg PO once daily. Doses may be administered as 150 mg PO BID if GI upset occurs.

**MAC prophylaxis for recurrence of opportunistic disease in HIV (in combination with ethambutol and a macrolide antibiotic [clarithromycin or azithromycin]):**

**Infant and child:** 5 mg/kg/24 hr PO once daily; **max. dose:** 300 mg/24 hr

**Adolescent and adult:** 300 mg PO once daily. Doses may be administered as 150 mg PO BID if GI upset occurs.

**MAC treatment:**

**Child:** 10–20 mg/kg/24 hr PO once daily; **max. dose:** 300 mg/24 hr as part of a multidrug regimen for severe disease.

**Adult:** 300 mg PO once daily; may be used in combination with azithromycin and ethambutol

**In combination with non-nucleoside reverse transcriptase inhibitors:**

**With efavirenz and no concomitant protease inhibitor:** 450 mg PO once daily or 600 mg PO 3 × per wk

**With nevirapine:** 300 mg PO 3 × per wk

*Continued*

RIFABUTIN *continued***MAC treatment (adult):****In combination with protease inhibitors:**

**With amprenavir, indinavir, or nelfinavir:** 150 mg PO once daily or 300 mg PO 3 × per wk

**With ritonavir-boosted regimens (e.g., saquinavir/ritonavir, or lopinavir/ritonavir):** 150 mg PO once every other day or 150 mg PO 3 × per week

**Should not be used** for MAC prophylaxis with active TB. May cause GI distress, discoloration of skin and body fluids (brown-orange color), and marrow suppression. **Use with caution** in renal and liver impairment. **Adjust dose in renal impairment (see Chapter 31).** May permanently stain contact lenses. Uveitis can occur when using high doses (>300 mg/24 hr in adults) in combination with macrolide antibiotics.

Rifabutin is an inducer of CYP 450 3A enzyme and is structurally similar to rifampin (similar drug interactions, see *Rifampin*). Clarithromycin, fluconazole, itraconazole, nevirapine, and protease inhibitors increase rifabutin levels. Efavirenz may decrease rifabutin levels. May decrease effectiveness of dapsone, delavirdine, nevirapine, amprenavir, indinavir, nelfinavir, saquinavir, itraconazole, warfarin, oral contraceptives, digoxin, cyclosporine, ketoconazole, and narcotics. Doses may be administered with food if patient experiences GI intolerance.

**RIFAMPIN**

Rimactane, Rifadin and other generics

**Antibiotic, antituberculous agent, rifamycin**



Yes



Yes



2



C

**Caps:** 150, 300 mg

**Oral suspension:** 10, 15, 25 mg/mL \Rx

**Injection:** 600 mg

**Staphylococcus aureus infections (as part of synergistic therapy with other anti-staphylococcal agents):**

**0–1 mo:**

**IV:** 10–20 mg/kg/24 hr ÷ Q12 hr

**PO:** 10–20 mg/kg/dose Q24 hr

**>1 mo:** 10–20 mg/kg/24 hr ÷ Q12 hr IV/PO; **max. dose:** 600 mg/24 hr

**Prosthetic valve endocarditis:** 15–20 mg/kg/24 hr IV/PO ÷ Q8 hr

**Adult:** 300–600 mg Q12 hr IV/PO

**Prosthetic valve endocarditis:** 300 mg Q8 hr IV/PO for a minimum of 6 wk in combination with antistaphylococcal penicillin with or without gentamicin

**Tuberculosis (see latest edition of the AAP Red Book for duration of therapy and combination therapy):** Twice weekly therapy may be used after 1–2 months of daily therapy.

**Infant, child and adolescent:**

**Daily therapy:** 10–20 mg/kg/24 hr ÷ Q12–24 hr IV/PO

**Twice weekly therapy:** 10–20 mg/kg/24 hr PO twice weekly

**Max. daily dose:** 600 mg/24 hr

**Adult:**

**Daily therapy:** 10 mg/kg/24 hr once daily PO

**Twice weekly therapy:** 10 mg/kg/24 hr once daily twice weekly

**Max. daily dose:** 600 mg/24 hr

**Prophylaxis for Neisseria meningitidis (see latest edition of AAP Red Book for additional information):**

**0–<1 mo:** 10 mg/kg/24 hr ÷ Q12 hr PO × 2 days

**≥1 mo:** 20 mg/kg/24 hr ÷ Q12 hr PO × 2 days

RIFAMPIN *continued***Adult:** 600 mg PO Q12 hr  $\times$  2 days**Max. dose (all ages):** 1200 mg/24 hr

**Never** use as monotherapy except when used for prophylaxis. Patients with latent tuberculosis infection should not be treated with rifampin and pyrazinamide because of risk of severe liver injury. Use is **not recommended** in porphyria. **Use with caution** in diabetes.

May cause GI irritation, allergy, headache, fatigue, ataxia, muscle weakness, confusion, fever, hepatitis, transient LFT abnormalities, blood dyscrasias, interstitial nephritis, and elevated BUN and uric acid. Causes red discoloration of body secretions, such as urine, saliva, and tears (which can permanently stain contact lenses). Induces hepatic enzymes (CYP 450 2C9, 2C19, and 3A4), which may decrease plasma concentration of digoxin, corticosteroids, buspirone, benzodiazepines, fentanyl, calcium channel blockers,  $\beta$ -blockers, cyclosporine, tacrolimus, itraconazole, ketoconazole, oral anticoagulants, barbiturates, and theophylline. May reduce effectiveness of oral contraceptives and antiretroviral agents (protease inhibitors and non-nucleoside reverse transcriptase inhibitors). Hepatotoxicity is a concern when used in combination with pyrazinamide and ritonavir-boosted saquinavir (**use is contraindicated**).

**Adjust dose in renal failure (see Chapter 31).** Reduce dose in hepatic impairment. Give 1 hr before or 2 hr after meals.

For *Haemophilus influenza* prophylaxis, see latest edition of AAP *Red Book*.

**RIMANTADINE**

Flumadine and generics

**Antiviral agent**

Yes



Yes



3



C

**Tabs:** 100 mg**Oral suspension:** 10 mg/1 mL \Rx 

**Influenza A prophylaxis (for at least 10 days after known exposure; usually for 6–8 wk during influenza A season or local outbreak):**

**Child:**1–9 yr: 5 mg/kg/24 hr PO once daily–BID; **max. dose:** 150 mg/24 hr **$\geq$  10 yr:**<40 kg: 5 mg/kg/24 hr PO  $\div$  BID; **max. dose:** 150 mg/24 hr **$\geq$  40 kg:** 100 mg/dose PO BID**Adult:** 100 mg PO BID

**Influenza A treatment (within 48 hr of illness onset):**

Use the aforementioned prophylaxis dosage  $\times$  5–7 days.

Resistance to influenza A and recommendations against the use for treatment and prophylaxis have been reported by the CDC. Check with local microbiology laboratories and the CDC for seasonal susceptibility/resistance.



Preferred over amantadine for influenza; lower incidence of adverse events. Individuals immunized with live attenuated influenza vaccine (e.g., FluMist) should not receive rimantadine prophylaxis for 14 days after the vaccine. Chemoprophylaxis does not interfere with immune response to inactivated influenza vaccine.

May cause GI disturbance, xerostomia, dizziness, headache, and urinary retention. CNS disturbances are less than with amantadine. **Contraindicated** in amantadine hypersensitivity. **Use with caution** in renal or hepatic insufficiency; dosage reduction may be necessary. A dosage reduction of 50% has been recommended in severe hepatic or renal impairment. Subjects with severe renal impairment have been reported to have an 81% increase in systemic exposure.

**RISPERIDONE**

Risperdal, Risperdal M-Tab, and Risperdal Consta

**Atypical antipsychotic, serotonin (5-HT<sub>2</sub>) and dopamine (D<sub>2</sub>) antagonist**

Yes



Yes



3



C

**Tabs:** 0.25, 0.5, 1, 2, 3, 4 mg**Oral solution:** 1 mg/mL (30 mL); may contain benzoic acid**Orally disintegrating tabs (Risperdal M-Tab and generics):** 0.5, 1, 2, 3, 4 mg; contains phenylalanine**Injection (Risperdal Consta):** 12.5, 25, 37.5, 50 mg (prefilled syringe with 20G, 2-inch needle and 2 mL diluent); for IM administration only**Irritability associated with autistic disorder:****5–16 yr (PO daily doses may be administered once daily–BID; patients experiencing somnolence may benefit from QHS or BID dosing or dose reduction):****Initial dose:****<20 kg:** 0.25 mg/24 hr PO for a minimum of 4 days; **use with caution** if < 15 kg (dosing recommendation is not established).**≥20 kg:** 0.5 mg/24 hr PO for a minimum of 4 days**Dose increment (if needed) after 4 days of initial dose:****<20 kg:** 0.5 mg/24 hr PO for a minimum of 14 days. If additional increments needed, increase dose by 0.25 mg/24 hr at intervals of at least 14 days.**≥20 kg:** 1 mg/24 hr PO for a minimum of 14 days. If additional increments needed, increase dose by 0.5 mg/24 hr at intervals of at least 14 days.**Max. daily dose for plateau of therapeutic effect (from one pivotal clinical trial):****<20 kg:** 1 mg/24 hr**≥20–45 kg:** 2.5 mg/24 hr**>45 kg:** 3 mg/24 hr**Bipolar mania:** Oral doses may be administered once daily–BID, and patients experiencing somnolence may benefit from QHS or BID dosing or dose reduction. Long-term use beyond 3 wk and doses (all ages) > 6 mg/24 hr have not been evaluated.**Child (10–17 yr):** Start with 0.5 mg/24 hr PO once daily (QAM or QHS). If needed, increase dose at intervals not <24 hr in increments of 0.5 or 1 mg/24 hr, as tolerated, up to a recommended dose of 2.5 mg/24 hr. Although efficacy has been demonstrated between 0.5–6 mg/24 hr, no additional benefit was seen above 2.5 mg/24 hr. Higher doses were associated with more adverse effects.**Adult:** Start with 2–3 mg PO once. Dosage increases or decreases of 1 mg/24 hr can be made at 24-hr intervals. Dosage range: 1–6 mg/24 hr.**Schizophrenia:** Oral doses may be administered once daily–BID, and patients experiencing somnolence may benefit from BID dosing (see remarks).**Adolescent (13–17 yr):** No data are available to support long-term use of >8 wk.**PO:** Start with 0.5 mg once daily (QAM or QHS). If needed, increase dose at intervals not <24 hr in increments of 0.5 to 1 mg/24 hr, as tolerated, to a recommended dose of 3 mg/24 hr. Although efficacy has been demonstrated between 1–6 mg/24 hr, no additional benefit was seen above 3 mg/24 hr. Doses >6 mg/24 hr have not been studied.**Adult:****PO:** Start with 1 mg BID on day 1; if tolerated, increase to 2 mg BID on day 2 and to 3 mg BID thereafter. Dosage increases or decreases of 1–2 mg can be made on a weekly basis if needed. Usual effective dose: 2–8 mg/24 hr. Doses above 16 mg/24 hr have not been evaluated.**IM:** Start with 25 mg Q2 wk; if no response, dose may be increased to 37.5 mg or 50 mg at 4-wk intervals. **Max. IM dose:** 50 mg Q2 wk.

RISPERIDONE *continued*

**Use with caution** in cardiovascular disorders, diabetes, renal or hepatic impairment

(dose reduction necessary), hypothermia or hyperthermia, seizures, breast cancer or other prolactin-dependent tumors, and dysphagia. Common side effects include abdominal pain and other GI disturbances, arthralgia, anxiety, dizziness, headache, insomnia, somnolence (use QHS dosing), EPS, cough, fever, pharyngitis, rash, rhinitis, sexual dysfunction, tachycardia, and weight gain. Weight gain, somnolence, and fatigue were common side effects reported in the autism studies. Priapism, hypothermia, sleep apnea syndrome, urinary retention, diabetes mellitus, and hypoglycemia have been reported in postmarketing reports.

In the presence of severe renal or hepatic impairment or risk for hypotension, the following adult dosing has been recommended: Start with 0.5 mg PO BID. Increase dose, if needed and tolerated, in increments no more than 0.5 mg BID. Increases to doses >1.5 mg BID should occur at intervals of at least 1 wk; slower titration may be required in some patients.

Limited studies in pediatric-related Tourette syndrome, schizophrenia, and aggressive behavior in psychiatric disorders are reported. Autistic disorder safety and efficacy in children <5 yr have not been established. If therapy has been discontinued for a period of time, therapy should be reinitiated with the same initial titration regimen.

Drug is a CYP 450 2D6 and 3A4 isoenzyme substrate. Concurrent use of isoenzyme inhibitors (e.g., fluoxetine, paroxetine, sertraline, cimetidine) and inducers (e.g., carbamazepine, rifampin, phenobarbital, phenytoin) may increase and decrease effects of risperidone, respectively. Alcohol, CNS depressants, and St. John's wort may potentiate drug's side effects. Risperidone may enhance hypotensive effects of levodopa and dopamine agonists.

Oral dosage forms may be administered with or without food. Oral solution can be mixed in water, coffee, orange juice, or low-fat milk but is incompatible with cola or tea. **Do not** split or chew the orally disintegrating tablet. Use IM suspension preparation within 6 hr after reconstitution.

**ROCURONIUM**

Zemuron and generics

**Nondepolarizing neuromuscular blocking agent**



Yes



No



?



C

**Injection:** 10 mg/mL (5, 10 mL)

**Use of a peripheral nerve stimulator to monitor drug effect is recommended.**

**Infant:**

**IV:** 0.5 mg/kg/dose; may repeat Q20–30 min PRN

**Child (3 mo–12 yr):**

**IV:** 0.6 mg/kg/dose  $\times$  1. If needed, give maintenance doses of 0.075–0.125 mg/kg/dose Q 20–30 min PRN when neuromuscular blockade returns to 25% of control. Alternatively, a maintenance continuous IV infusion may be used starting at 7–12 mcg/kg/min (use lower end for children 2–11 yr) when neuromuscular blockade returns to 10% of control.

**Adolescent and adult:**

**IV:** Start with 0.6–1.2 mg/kg/dose  $\times$  1. If needed, maintenance doses at 0.1–0.2 mg/kg/dose Q20–30 min PRN. Alternatively, a maintenance continuous IV infusion may be used starting at 10–12 mcg/kg/min (range, 4–16 mcg/kg/min).

**Use with caution** in hepatic impairment and history of anaphylaxis with other neuromuscular blocking agents. Hypertension, hypotension, arrhythmia, tachycardia, nausea, vomiting, bronchospasm, wheezing, hiccups, rash, and edema at injection site may occur. Myopathy after long-term use in an ICU, and QT-interval prolongation in pediatric patients receiving general anesthetic agents have been reported. Increased neuromuscular blockade may occur



*Continued*



ROCURONIUM *continued*

with concomitant use of aminoglycosides, clindamycin, tetracycline, magnesium sulfate, quinine, quinidine, succinylcholine, and inhalation anesthetics (for continuous infusion, reduce infusion by 30%–50% at 45–60 min after intubating dose).

Caffeine, calcium, carbamazepine, phenytoin, phenylephrine, azathioprine, and theophylline may reduce neuromuscular blocking effects.

Use must be accompanied by adequate anesthesia or sedation. Peak effects occur in 0.5–1 min for children and in 1–3.7 min for adults. Duration of action: 30–40 min in children and 20–94 min in adults (longer in geriatrics). Recovery time in children 3 mo–1 yr is similar to adults. To prevent residual paralysis, extubate patient **only** after sufficiently recovered from neuromuscular blockade. In obese patients, use actual body weight for dosage calculation.

**SALMETEROL**

Serevent Diskus

***β<sub>2</sub>-Adrenergic agonist (long acting)***

No



No



2



C

**Dry powder inhalation (DPI; Diskus):** 50 mcg/inhalation (28, 60 inhalations); contains lactose

**In combination with fluticasone:** See *Fluticasone Propionate and Salmeterol*

**Persistent asthma (see remarks):**

≥4 yr and adult: 1 inhalation (50 mcg) Q12 hr

**Prevention of exercise-induced bronchospasm:**

≥4 yr and adult: 1 inhalation 30–60 min before exercise. Additional doses should not be used for another 12 hr. Patients who are already using Q12 hr dosing for persistent asthma should not use additional salmeterol doses for this indication and use alternative therapy (e.g., cromolyn) before exercise.

For long-term asthma control, should be used in combination with inhaled corticosteroids.

**Should not be used to relieve symptoms of acute asthma.** It is long acting and has its onset of action in 10–20 min, with a peak effect at 3 hr. May be used QHS (1 inhalation of the DPI) for nocturnal symptoms. Salmeterol is a chronic medication and is **not** used in similar fashion to short-acting β-agonists (e.g., albuterol). Patients already receiving salmeterol Q12 hr should not use additional doses for prevention of exercise-induced bronchospasm; consider alternative therapy. Asthma exacerbations or hospitalizations were reported to be lower when used with an inhaled corticosteroid.

**WARNING: Long-acting β<sub>2</sub>-agonists may increase risk of asthma-related death.** A subgroup analysis suggested higher risk in African-American patients compared with Caucasians. Use salmeterol only as additional therapy for patients not adequately controlled on other asthma-controller medications (e.g., low- to medium-dose inhaled corticosteroids) or whose disease severity clearly requires initiation of treatment with two maintenance therapies.

**Should not be used** in conjunction with an inhaled long-acting β<sub>2</sub>-agonist and is **not** a substitute for inhaled or systemic corticosteroid. Use with strong CYP 3A4 inhibitors (e.g., ketoconazole, HIV protease inhibitors, clarithromycin, itraconazole, nefazodone, and telithromycin) are not recommended owing to risk for cardiovascular adverse events (e.g., QTc prolongation, tachycardia). Salmeterol is a P450 3A4 substrate.

Proper patient education is essential. Side effects are similar to albuterol. Hypertension and arrhythmias have been reported. See Chapter 24 for recommendations for asthma controller therapy.

**SCOPOLAMINE HYDROBROMIDE**

Transderm Scop, Isopto Hyoscine, and generics

**Anticholinergic agent**

Yes



Yes



2



C

**Injection:** 0.4 mg/mL (1 mL); may contain alcohol**Transdermal (Transderm Scop):** 1.5 mg/patch (4s, 10s and 24s); delivers  $\approx$  1 mg over 3 days**Ophthalmic solution (Isopto Hyoscine):** 0.25% (5 mL); contains benzalkonium chloride**Antiemetic (SC/IM/IV):****Child:** 6 mcg/kg/dose Q6–8 hr PRN; **max. dose:** 300 mcg/dose**Adult:** 0.32–0.65 mg/dose Q6–8 hr PRN**Transdermal ( $\geq$  12 yr) (see remarks):****Motion sickness:** Apply patch behind the ear at least 4 hr before exposure to motion; remove after 72 hr.**Antiemetic before surgery:** Apply patch behind the ear the evening before surgery. Remove patch 24 hr after surgery.**Antiemetic before cesarean section:** Apply patch behind the ear 1 hr before surgery to minimize infant exposure. Remove patch 24 hr after surgery.**Ophthalmic (see remarks):****Refraction:****Child:** 1 drop BID for 2 days before procedure**Adult:** 1–2 drop(s) 1 hr before procedure**Iridocyclitis:****Child:** 1 drop up to TID**Adult:** 1–2 drop(s) up to TID

Toxicities similar to atropine. **Contraindicated** in urinary or GI obstruction and glaucoma. **Use with caution** in hepatic or renal dysfunction, cardiac disease, seizures, or psychoses. May cause dry mouth, drowsiness, and blurred vision.

Transdermal route should **NOT** be used in children  $<12$  yr. Drug withdrawal symptoms (nausea, vomiting, headache, vertigo) have been reported after removal of transdermal patch in patients using patch for  $>3$  days. For perioperative use, patch should be kept in place for 24 hr after surgery. Systemic effects have been reported with both transdermal and ophthalmic preparations. Compress nasolacrimal ducts to minimize systemic effects when using ophthalmic preparations.

**SELENIUM SULFIDE**

Selsun and others

**Topical antiseborrheic agent**

No



No



2



C

**Lotion/Shampoo:** 1% [OTC] (120, 210, 325, 400 mL); some shampoo products are available with conditioner.**Topical lotion:** 2.5% (120 mL)**Topical aerosol foam:** 2.25% (70 g) **$\geq 2$  yr and adult:****Seborrhea/dandruff:** Massage 5–10 mL of shampoo into wet scalp and leave on scalp for 2–3 min. Rinse thoroughly and repeat. Shampoo twice weekly  $\times$  2 weeks. Maintenance applications once every 1–4 wk.**Tinea versicolor:** Apply 2.5% lotion to affected areas of skin. Allow to remain on skin  $\times$  10 min. Rinse thoroughly. Repeat once daily  $\times$  7 days. Follow with monthly applications for 3 mo to prevent recurrences.

Continued

SELENIUM SULFIDE *continued*

Rinse hands and body well after treatment. May cause local irritation, hair loss, and hair discoloration. **Avoid** eyes, genital areas, and skin folds. Shampoo may be used for tinea capitis to reduce risk of transmission to others (does not eradicate tinea infection).

For tinea versicolor, 15%–25% sodium hyposulfite or thiosulfate (Tinver lotion) applied to affected areas BID  $\times$  2–4 wk is an alternative. Topical antifungals (e.g., clotrimazole, miconazole) may be used for small focal infections. **Do not use** for tinea versicolor during pregnancy.



## SENNA/SENNOSIDES

Senokot, Senna-Gen, Lax-Pills, and many others

**Laxative, stimulant**



No



No



1



C

**Based on mg of senna (all products are OTC):**

**Granules:** 326 mg/tsp

**Oral syrup:** 176 mg/5 mL, 218 mg/5 mL (60 mL, 240 mL)

**Tabs:** 187, 217, 374 mg

187 mg senna extract is approximately 8.6 mg sennosides.

**Based on mg of sennosides (all products are OTC):**

**Granules:** 15 mg/tsp, 20 mg/tsp

**Oral syrup:** 8.8 mg/5 mL (60, 240 mL)

**Tabs:** 8.6, 15, 17.2, 25 mg

**Chewable tabs:** 15 mg

8.6 mg sennosides is approximately 187 mg senna extract.

**Constipation:****Dosing based on mg senna:****Child:**

**Oral:** 10–20 mg/kg/dose PO QHS (to **max. dose** as shown below) or dosage by age:

**1 mo–1 yr:** 55–109 mg PO QHS to **max. dose** of 218 mg/24 hr

**1–5 yr:** 109–218 mg PO QHS to **max. dose** of 436 mg/24 hr

**5–15 yr:** 218–436 mg PO QHS to **max. dose** of 872 mg/24 hr

**Adult:**

**Granules:** 326 mg (1 tsp) PO at bedtime; **max. dose:** 652 mg (2 tsp) BID

**Syrup:** 436–654 mg PO at bedtime; **max.** 654 mg (15 mL) BID

**Tabs:** 374 mg PO at bedtime; **max.** 748 mg BID

**Dosing based on mg sennosides:****Child:****Syrup:**

**1 mo–2 yr:** 2.2–4.4 mg (1.25–2.5 mL) PO QHS to **max. dose** of 8.8 mg/24 hr

**2–5 yr:** 4.4–6.6 mg (2.5–3.75 mL) PO QHS to **max. dose** of 6.6 mg BID

**6–12 yr:** 8.8–13.2 mg (5–7.5 mL) PO QHS to **max. dose** of 13.2 mg BID

**Tabs:**

**2–5 yr:** 4.3 mg PO QHS to **max. dose** of 8.6 mg BID

**6–12 yr:** 8.6 mg PO QHS to **max. dose** of 17.2 mg BID

**>12 yr and adult:**

**Granules:** 15 mg PO QHS to **max. dose** of 30 mg BID

**Syrup:** 17.6–26.4 mg (10–15 mL) PO QHS to **max. dose** of 26.4 mg BID

**Tabs:** 17.2 mg PO QHS to **max. dose** of 34.4 mg BID

Effects occur within 6–24 hr after oral administration. Prolonged use (>1 wk) should be **avoided**; may lead to dependency. May cause nausea, vomiting, diarrhea, abdominal cramps. Active metabolite stimulates Auerbach's plexus. Syrup may be administered with juice, milk, or mixed with ice cream. Granules may be sprinkled onto food or mixed with drinks.



**SERTRALINE HCL**

Zoloft and generics

**Antidepressant (selective serotonin reuptake inhibitor)**

Yes



Yes



2



C

**Tabs:** 25, 50, 100 mg**Oral concentrate solution:** 20 mg/mL (60 mL); contains alcohol and menthol**Depression:****Child ≥ 6–12 yr (data limited in this age group):** Start at 12.5–25 mg PO once daily.May increase dosage by 25 mg at 1-wk intervals up to a **max. dose** of 200 mg/24 hr.**Child ≥ 13 yr and adult:** Start at 25–50 mg PO once daily. May increase dosage by 50 mg at 1-wk intervals up to a **max. dose** of 200 mg/24 hr.**Obsessive-compulsive disorder:****Child ≥ 6–12 yr:** Start at 25 mg PO once daily. May increase dosage by 25 mg at 3–4 day intervals or by 50 mg at 7-day intervals up to a **max. dose** of 200 mg/24 hr.**Child ≥ 13 yr and adult:** Start at 50 mg PO once daily. May increase dosage by 50 mg at 1-wk intervals up to **max. dose** of 200 mg/24 hr.

Drug is **contraindicated** in combination (or within 14 days of discontinuing use) with an MAOI (e.g., linezolid or IV methylene blue) or pimozone (increases adverse/toxic effects of pimozone). **Use with caution** in patients with abnormal bleeding, SIADH, and hepatic or renal impairment. Adverse effects include nausea, diarrhea, tremor, and increased sweating. Hyponatremia, diabetes mellitus, and platelet dysfunction have been reported. Monitor for clinical worsening of depression and suicidal ideation/behavior after initiation of therapy or after dose changes. Use during late third trimester of pregnancy may increase risk for newborn withdrawal symptoms and persistent pulmonary hypertension in the newborn.

Use with drugs that interfere with hemostasis (e.g., NSAIDs, aspirin, warfarin) may increase risk for GI bleeds. Use with warfarin may increase PT. Inhibits the CYP 450 2D6 drug metabolizing enzyme. Serotonin syndrome may occur when taken with SSRIs (e.g., amitriptyline, amphetamines, buspirone, dihydroergotamine, sumatriptan, sympathomimetics).

Mix oral concentrate solution with 4 oz of water, ginger ale, lemon/lime soda, lemonade, or orange juice. After mixing, a slight haze may appear; this is normal. This dosage form should be **used cautiously** in patients with latex allergy; dropper contains dry natural rubber.

**SILDENAFIL**

Revatio, Viagra, and generics

**Phosphodiesterase type 5 (PDE5) inhibitor**

Yes



Yes



?



B

**Tabs:****Revatio and generic:** 20 mg**Viagra:** 25, 50, 100 mg**Oral suspension:** 2.5 mg/mL **Revatio:** 10 mg/mL (112 mL)**Injection:****Revatio:** 0.8 mg/mL (12.5 mL)**Pulmonary hypertension:****Neonate (limited data from case reports and small clinical trials):**

**PO:** Several dosages have been reported and have ranged from 0.5–3 mg/kg/dose Q6–12 hr PO. A single ≈ 0.3 mg/kg/dose PO has been used in selected patients to facilitate weaning from inhaled nitric oxide.

**IV (case report from 4 neonates > 34 wk' gestation and < 72 hr old):** Start with 0.4 mg/kg/dose IV over 3 hr, followed by a continuous infusion of 1.6 mg/kg/24 hr (0.067 mg/kg/hr) for up to 7 days.

Continued

SILDENAFIL *continued***Infant and child:**

**PO:** Several dosages have been reported. Start at 0.25–0.5 mg/kg/dose Q4–8 hr PO; if needed and tolerated, increase to 1 mg/kg/dose Q4–8 hr PO. Doses as high as 2 mg/kg/dose Q4 hr PO have been given in case reports. A single  $\approx$  0.4 mg/kg/dose PO has been used in selected patients to facilitate weaning from inhaled nitric oxide.

**Child 1–17 yr (results from a 16-wk dose-ranging study in 235 treatment-naïve children  $\geq$  8 kg with pulmonary arterial hypertension [see remarks]):**

**PO:**

**$\geq$ 8–20 kg:** 10–20 mg TID

**>20–45 kg:** 20–40 mg TID

**>45 kg:** 40–80 mg TID

**Pulmonary arterial hypertension:****Adult:**

**PO:** 20 mg TID (taken at least 4–6 hr apart)

**IV:** 10 mg TID

**Contraindicated** with concurrent use of nitrates (e.g., nitroglycerin) and other nitric oxide donors; potentiates hypotensive effects. **Use with caution** in sepsis (high levels of cGMP may potentiate hypotension), hypotension, sickle cell (use not established), anemias, and with concurrent CYP 450 3A4–inhibiting medications (see discussion that follows) and antihypertensive medications. Hepatic insufficiency or severe renal impairment (GFR < 30 mL/min) significantly reduces sildenafil clearance.

Findings from the dose-ranging study in 1- to 17-year-olds with pulmonary arterial hypertension found an association of increased mortality risk with long-term use (>2 yr). Headache, pyrexia, URTIs, vomiting, and diarrhea were the most frequently reported side effects in this study. Optimal dosing based on age and body weight has yet to be determined.

In adults, a transient impairment of color discrimination may occur; this effect could increase risk of severe retinopathy of prematurity in neonates. Common side effects reported in adults have included flushing, rash, diarrhea, indigestion, headache, abnormal vision, and nasal congestion. Hearing loss has been reported.

Sildenafil is a substrate for CYP 450 3A4 (major) and 2C8/9 (minor). Azole antifungals, cimetidine, ciprofloxacin, clarithromycin, erythromycin, nicardipine, propofol, protease inhibitors, quinidine, verapamil, and grapefruit juice may increase effects/toxicity of sildenafil. Bosentan, efavirenz, carbamazepine, phenobarbital, phenytoin, rifampin, St. John's wort, and high-fat meals decrease sildenafil's effects.

**SILVER SULFADIAZINE**

Silvadene, Thermazene, SSD Cream, and generics

**Topical antibiotic**

Yes



Yes



3



B

**Cream:** 1% (20, 25, 50, 85, 400, 1000 g); contains methylparabens and propylene glycol

**Child ( $\geq$ 2 mo) and adult:** Cover affected areas completely once daily–BID. Apply cream to a thickness of 1/16 inch using sterile technique.

**Contraindicated** in premature infants and infants  $\leq$  2 mo of age owing to concerns of kernicterus; and pregnancy (approaching term). **Use with caution** in G6PD and renal and hepatic impairment. Discard product if cream has darkened. Significant systemic absorption may occur in severe burns. Adverse effects include pruritus, rash, bone marrow suppression, hemolytic anemia, and interstitial nephritis. **NOT** for ophthalmic use. Dressing may be used but is **not** necessary. See Chapter 4 for more information.

**SIMETHICONE**

Mylicon, Phazyme, Mylanta Gas, Gas-X and generics

**Antiflatulent**

No



No



1



C

All dosage forms available OTC

**Oral drops:** 40 mg/0.6 mL (30 mL)**Caps:** 125, 180 mg**Tabts:** 60, 95 mg**Chewable tabs:** 80, 125 mg**Strip, orally disintegrating:** 40 mg (16s), 62.5 mg (18s, 30s); may contain alcohol**Infant and child < 2 yr:** 20 mg PO QID PRN; **max. dose:** 240 mg/24 hr**2–12 yr:** 40 mg PO QID PRN**> 12 yr and adult:** 40–250 mg PO QPC and QHS PRN; **max. dose:** 500 mg/24 hr

Efficacy has not been demonstrated for treating infant colic. **Avoid** carbonated beverages and gas-forming foods. Oral liquid may be mixed with water, infant formula, or other suitable liquids for ease of oral administration.

**SIROLIMUS**

Rapamune and generics

**Immunosuppressant agent**

Yes



Yes



3



C

**Tabts:** 0.5, 1, 2 mg**Oral solution:** 1 mg/mL (60 mL); contains 1.5%–2.5% ethanol

**Child ≥ 13 yr and < 40 kg:** 3 mg/m<sup>2</sup>/dose PO × 1 immediately after transplantation, followed by 1 mg/m<sup>2</sup>/24 hr PO ÷ Q12–24 hr on the next day. Adjust dose to achieve desired trough blood levels.

**Adult:****Patients at low/moderate immunologic risk:****In combination with cyclosporine (adjust dose to achieve desired trough blood levels):**

**< 40 kg:** 3 mg/m<sup>2</sup>/dose PO × 1 immediately after transplantation, followed by 1 mg/m<sup>2</sup>/dose PO once daily on the next day

**≥ 40 kg:** 6 mg PO × 1 immediately after transplantation, followed by 2 mg PO once daily on the next day

**Patients at high immunologic risk:****In combination with cyclosporine (withdrawal of cyclosporine is not recommended):** 15 mg

PO × 1 immediately after transplantation, followed by 5 mg PO once daily on the next day. Adjust dose to achieve desired trough blood levels.

Increased susceptibility to infection and development of lymphoma may result from immunosuppression. **Fatal** bronchial anastomotic dehiscence has been reported in lung transplantation. Excess mortality, graft loss, and hepatic artery thrombosis have been reported in liver transplantation when used with tacrolimus. Patients with the greatest amount of urinary protein excretion before sirolimus conversion were those whose protein excretion increased the most after conversion. Increased risk of BK virus–associated nephropathies have been reported. Increased mortality in stable liver transplant patients has been reported after conversion from a calcineurin inhibitor–based regimen to sirolimus.

Monitor whole blood trough levels (just before a dose at steady state), especially with pediatric patients, hepatic impairment, concurrent use of CYP 450 3A4 and/or P-gp inducers and inhibitors, and/or if cyclosporine dosage is markedly changed or discontinued. Steady state is generally



Continued

SIROLIMUS *continued*

achieved after 5–7 days of continuous dosing. **Interpretation will vary based on specific treatment protocol and assay methodology (HPLC vs. immunoassay vs. LC/MS/MS).** Younger children may exhibit faster sirolimus clearance compared with adolescents.

Sirolimus is a substrate for CYP 450 3A4 and P-gp. Cyclosporine, diltiazem, protease inhibitors, erythromycin, grapefruit juice, and other inhibitors of CYP 3A4 may increase toxicity of sirolimus. Phenobarbital, carbamazepine, phenytoin, and St. John's wort may decrease effects of sirolimus. Strong inhibitors (e.g., azole antifungals and clarithromycin) and strong inducers (e.g., rifamycins) are **not recommended**.

Hypertension, peripheral edema, increased serum creatinine, dyspnea, epistaxis, headache, anemia, thrombocytopenia, hyperlipidemia, hypercholesterolemia, and arthralgia may occur. Progressive multifocal leukoencephalopathy (PML), ovarian cysts, and menstrual disorders have been reported. Urinary tract infections have been reported in pediatric renal transplant patients with high immunologic risk.

Two mg of the oral solution has been demonstrated to be clinically equivalent to 2-mg tablets.

However, it is not known whether they are still therapeutically equivalent at higher doses. Reduce maintenance dosage by  $\frac{1}{3}$  in the presence of hepatic function impairment. Administer doses consistently with or without food. When administered with cyclosporine, give dose 4 hr after cyclosporine. **Do not** crush or split tablets. Measure the oral liquid dosage form with an amber oral syringe and dilute in a cup with 60 mL of water or orange juice only. Take dose immediately after mixing, add/mix additional 120 mL diluent into the cup, and drink immediately after mixing.

**SODIUM BICARBONATE**

Neut and many generics

**Alkalinizing agent, electrolyte**



No



Yes



1



C

**Injection:** 4% (Neut) (0.48 mEq/mL) (5 mL), 4.2% (0.5 mEq/mL) (5, 10 mL), 7.5% (0.89 mEq/mL) (50 mL), 8.4% (1 mEq/mL) (10, 50 mL)

**Tablets:** 325 mg (3.8 mEq), 650 mg (7.6 mEq)

**Powder:** 120, 480 g; contains 30 mEq Na<sup>+</sup> per  $\frac{1}{2}$  teaspoon

Each 1 mEq bicarbonate provides 1 mEq Na<sup>+</sup>.

**Cardiac arrest:** See inside front cover.

**Correction of metabolic acidosis:** Calculate patient's dose with the following formulas.

**Neonate, infant and child:**

$$\text{HCO}_3^- (\text{mEq}) = 0.3 \times \text{weight (kg)} \times \text{base deficit (mEq/L), OR}$$

$$\text{HCO}_3^- (\text{mEq}) = 0.5 \times \text{weight (kg)} \times [24 - \text{serum HCO}_3^- (\text{mEq/L})]$$

**Adult:**

$$\text{HCO}_3^- (\text{mEq}) = 0.2 \times \text{weight (kg)} \times \text{base deficit (mEq/L), OR}$$

$$\text{HCO}_3^- (\text{mEq}) = 0.5 \times \text{weight (kg)} \times [24 - \text{serum HCO}_3^- (\text{mEq/L})]$$

**Urinary alkalization (titrate dose accordingly to urine pH):**

**Child:** 84–840 mg (1–10 mEq)/kg/24 hr PO  $\div$  QID

**Adult:** 4 g (48 mEq)  $\times$  1, followed by 1–2 g (12–24 mEq) PO Q4 hr. Doses up to 16 g (192 mEq)/24 hr have been used.

**Contraindicated** in respiratory alkalosis, hypochloremia, and inadequate ventilation during cardiac arrest. **Use with caution** in CHF, renal impairment, cirrhosis, hypocalcemia, hypertension, and concurrent corticosteroids. Maintain high urine output. Monitor acid-base balance and serum electrolytes. May cause hypernatremia (contains sodium), hypokalemia, hypomagnesemia, hypocalcemia, hyperreflexia, edema, and tissue necrosis (extravasation). Oral route of administration may cause GI discomfort and gastric rupture from gas production.



SODIUM BICARBONATE *continued*

For direct IV administration (cardiac arrest) in neonates and infants, use the 0.5 mEq/mL (4.2 %) concentration or dilute the 1 mEq/mL (8.4 %) concentration 1:1 with sterile water for injection and infuse at a rate **no greater than** 10 mEq/min. The 1 mEq/mL (8.4 %) concentration may be used in children and adults for direct IV administration.

For IV infusions (for all ages), dilute to a **max. concentration** of 0.5 mEq/mL in dextrose or sterile water for injection, and infuse over 2 hr using a **max. rate** of 1 mEq/kg/hr.

Sodium bicarbonate should **not** be mixed with or be in contact with calcium, norepinephrine, or dobutamine.

**SODIUM CHLORIDE—INHALED PREPARATIONS**

Hypersal, Simply Saline, Ocean, Ayr Saline, Rhinaris, and many other brands and generics

**Electrolyte, inhalation**



No



No



1



C

**Nebulized solution:** 0.9% (3, 5, 15 mL), 3% (4, 15 mL), 6% (4 mL), 7% (4 mL), 10% (4, 15 mL)

**Hypersal (preservative-free):** 3.5% (4 mL), 7% (4 mL)

**Nasal solution spray/drops/mist [OTC]:** 0.125% (15 mL), 0.2% (30 mL), 0.65% (15, 30, 45 mL), 0.9% (45, 90 mL), 3% (44 mL)

**Nasal gel:** 0.2% (28.4 g), 0.65% (30 g), 3% (20 g)

**Intranasal as moisturizer:**

**Child and adult:**

**Spray/Mist:** 2–6 sprays into each nostril Q2 hr PRN

**Drops:** 2–6 drops into each nostril Q2 hr PRN

**Nasal gel:** Use PRN to relieve nasal discomfort. Use at bedtime helps in preventing drying and crusting.

**Cystic fibrosis (pretreatment with albuterol is recommended to prevent bronchospasms [see remarks]):**

**≥6 yr and adult:** Nebulize 4 mL of 7% solution once daily–BID. If unable to tolerate the 7% strength, lower strengths of 3%, 3.5%, or 5% may be used.

**Acute viral bronchiolitis (for hospitalized patients only; pretreatment with albuterol is recommended to prevent bronchospasms [see remarks]):**

**Infant (>34 week' gestation up to 18 mo old):** Nebulize 4 mL of 3% solution Q2 hr × 3 doses, followed by Q4 hr × 5 doses, followed by Q6 hr until discharge.

**INTRANASAL USE:** May be used as a nasal wash for sinuses, restore moisture, thin nasal secretions, or relieve dry, crusted, and inflamed nasal membranes from colds, low humidity, allergies, nasal decongestant overuse, minor nose bleeds, and other irritations. Nasal administration instructions:

**Nasal drops:** Tilt head back and hold bottle upside down.

**Nasal spray:** Hold head in upright position and give short, firm squeezes into each nostril. Sniff deeply.

**Nasal gel:** Apply around nostrils, under nose, or in nostrils as needed to help relieve discomfort.

**NEBULIZATION:** Hypertonic solutions lowers sputum viscosity and enhances mucociliary clearance.

**Cystic fibrosis:** Improves FEV<sub>1</sub> and reduces pulmonary exacerbation frequency. May cause bronchospasm, cough, pharyngitis, hemoptysis, and acute decline in pulmonary function (administer first dose in a medical facility). It is recommended to withhold therapy in the presence of massive hemoptysis.

**Acute viral bronchiolitis:** Reduces length of hospitalization when compared to normal saline. May cause acute bronchospasm and local irritation.





**SODIUM PHOSPHATE**

Fleet Enema, Fleet Pedia-Lax, Fleet Enema Extra, Fleet Phospho-Soda, OsmoPrep, and generics

**Laxative, enema/oral**



No



Yes



2



C

**Enema [OTC]:**

7 g dibasic sodium phosphate and 19 g monobasic sodium phosphate/118 mL; contains 4.4 g sodium per 118 mL

**Pediatric size (Fleet Pedia-Lax):** 66 mL

**Adult size (Fleet Enema):** 133 mL

7 g dibasic sodium phosphate and 19 g monobasic sodium phosphate/197 mL; contains 4.4 g sodium per 197 mL

**Fleet Enema Extra:** 230 mL

**Oral solution (Fleet Phospho-Soda and generics) [OTC]:** 2.4 g monobasic sodium phosphate and 0.9 g dibasic sodium phosphate/5 mL (45 mL); contains 96.4 mEq Na per 20 mL and 62.25 mEq phosphate/5 mL

**Oral tablets (OsmoPrep):** 1.5 g

Not to be used for phosphorus supplementation (see *Phosphorus Supplements*).

**Enema (see remarks):**

**2–4 yr:** 33 mL enema (half of Fleet Pedia-Lax)  $\times$  1

**5–11 yr:** 66 mL enema (Fleet Pedia-Lax)  $\times$  1

**$\geq 12$  yr and adult:** 133 mL enema (Fleet Enema) *OR* 230 mL enema (Fleet enema Extra)  $\times$  1

**Oral laxative (Fleet Phospho-Soda); mix with a full glass of water:**

**5–9 yr:** 7.5 mL PO  $\times$  1

**10–11 yr:** 15 mL PO  $\times$  1

**$\geq 12$  yr and adult:** 15–45 mL PO  $\times$  1

**Contraindicated** in patients with severe renal failure, megacolon, bowel obstruction, and CHF. May cause hyperphosphatemia, hypernatremia, hypocalcemia, hypotension, dehydration, and acidosis. **Avoid** retention of enema solution and **do not exceed** recommended doses; may lead to severe electrolyte disturbances due to enhanced systemic absorption. Colonic mucosal aphthous ulceration should be considered when interpreting colonoscopy findings with use in patients with known or suspected IBD. Rare but serious form of kidney failure (acute phosphate nephropathy) has been reported with use of bowel-cleansing preparations such as Fleet Phospho-Soda.

**Onset of action:** PO, 3–6 hr; PR, 2–5 min

**SODIUM POLYSTYRENE SULFONATE**

Kayexalate, SPS, Kionex, and generics

**Potassium-removing resin**



No



Yes



2



C

**Powder:** 454 g

**Oral suspension:** 15 g/60 mL (60, 120, 500 mL); contains 21.5 mL sorbitol per 60 mL and 0.1%–0.3% alcohol

Contains 4.1 mEq Na<sup>+</sup>/g drug

**NOTE:** Suspension may be given PO or PR. Practical exchange ratio is 1 mEq K per 1 g resin. May calculate dose according to desired exchange (see remarks).

**Infant and child:**

**PO:** 1 g/kg/dose Q6 hr

**PR:** 1 g/kg/dose Q2–6 hr. Dosing by practical exchange (1 mEq K per 1 g resin) has been recommended for infants and smaller children.

SODIUM POLYSTYRENE SULFONATE *continued***Adult:****PO:** 15 g once daily–QID**PR:** 30–50 g Q6 hr

**Contraindicated** in obstructive bowel disease, neonates with reduced gut motility, and oral administration in neonates. **Use cautiously** in presence of renal failure, CHF, hypertension, or severe edema. May cause hypokalemia, hyponatremia, hypomagnesemia, and hypocalcemia. Cases of colonic necrosis, GI bleeding, ischemic colitis, and perforation have been reported with concomitant use of sorbitol in patients with GI risk factors (prematurity, history of intestinal disease or surgery hypovolemia, and renal insufficiency/failure). Use in neonates generally **not recommended** owing to complication concerns for hyponatremia and NEC.

1 mEq Na delivered for each mEq K removed. **Do not administer** with antacids or laxatives containing  $Mg^{2+}$  or  $Al^{3+}$ ; systemic alkalosis may result. Retain enema in colon for at least 30–60 min.

**SPIRONOLACTONE**

Aldactone and generics

**Diuretic, potassium sparing**

Yes



Yes



2



C/D

**Tabs:** 25, 50, 100 mg**Oral suspension:** 1, 2, 2.5, 5, 10, 25 mg/mL **Diuretic:****Neonate:** 1–3 mg/kg/24 hr ÷ once daily–BID PO**Child:** 1–3.3 mg/kg/24 hr ÷ BID–QID PO; **max. dose:** 100 mg/24 hr**Adult:** 25–200 mg/24 hr ÷ once daily–BID PO (see remarks); **max.** 200 mg/24 hr**Diagnosis of primary aldosteronism:****Child:** 125–375 mg/m<sup>2</sup>/24 hr ÷ once daily–BID PO**Adult:** 400 mg once daily PO × 4 days (short test) or 3–4 wk (long test), then 100–400 mg once daily–BID maintenance**Hirsutism in women:****Adult:** 50–200 mg/24 hr ÷ once daily–BID PO

**Contraindicated** in Addison's disease, hyperkalemia, use with eplerenone, or severe renal failure (see Chapter 31). **Use with caution** in dehydration, hyponatremia, and renal or hepatic dysfunction. May cause hyperkalemia (especially with severe heart failure), GI distress, rash, lethargy, dizziness, and gynecomastia. May potentiate ganglionic blocking agents and other antihypertensives. Monitor potassium levels and be aware of other  $K^+$  sources,  $K^+$ -sparing diuretics, and ACE inhibitors (all can increase  $K^+$ ).

Do not use with other medications known to cause hyperkalemia (e.g., ACE inhibitors, angiotensin II antagonists, aldosterone blockers, and other potassium-sparing diuretics). Hyperkalemic metabolic acidosis has been reported with concurrent cholestyramine use. May cause false elevation in serum digoxin levels measured by radioimmunoassay.

Although TID–QID regimens have been recommended, data suggest once daily–BID dosing to be adequate. Pregnancy category changes to "D" if used in pregnancy-induced hypertension.

**STREPTOMYCIN SULFATE**

Various generics

**Antibiotic, aminoglycoside; antituberculous agent**

No



Yes



2



D

Powder for injection: 1 g

**Tuberculosis:** Use as part of multidrug regimen; see latest edition of AAP *Red Book*.**Infant, child, and adolescent:****Daily therapy:** 20–40 mg/kg/24 hr IM once daily; **max. daily dose:** 1 g/24 hr**Twice-weekly therapy (under direct observation):** 20–40 mg/kg/dose IM twice weekly; **max. daily dose:** 1.5 g/24 hr**Adult:****Daily therapy:** 15 mg/kg/24 hr IM once daily; **max. daily dose:** 1 g/24 hr**Twice-weekly therapy (under direct observation):** 25–30 mg/kg/dose IM twice weekly; **max. daily dose:** 1.5 g/24 hr**Brucellosis, tularemia, plague and rat bite fever:** See latest edition of the *Red Book*.

**Contraindicated** with aminoglycoside and sulfite hypersensitivity. **Use with caution** in preexisting vertigo, tinnitus, hearing loss, and neuromuscular disorders. Drug is administered via deep IM injection **only**. Follow auditory status. May cause CNS depression, other neurologic problems, myocarditis, serum sickness, nephrotoxicity, and ototoxicity. Concomitant neurotoxic, ototoxic, or nephrotoxic drugs and dehydration may increase risk for toxicity.

Therapeutic levels: Peak 15–40 mg/L; trough: <5 mg/L. Recommended serum sampling time at steady state: trough within 30 min before third consecutive dose and peak 30–60 min after administration of third consecutive dose. Therapeutic levels are **not** achieved in CSF.

**Adjust dose in renal failure (see Chapter 31).****SUCCIMER**

Chemet, DMSA [dimercaptosuccinic acid]

**Chelating agent**

Yes



Yes



?



C

**Cap:** 100 mg**Lead chelation, child:**10 mg/kg/dose (or 350 mg/m<sup>2</sup>/dose) PO Q8 hr × 5 days, then 10 mg/kg/dose (or 350 mg/m<sup>2</sup>/dose) PO Q12 hr × 14 days

Manufacturer recommendation (see following table):

Weight (kg)	Dose (mg) Q8 hr × 5 Days, Followed by Same Dose Q12 hr × 14 Days
8–15	100
16–23	200
24–34	300
35–44	400
≥45	500

**Use caution** in patients with compromised renal or hepatic function. Repeated courses may be necessary. Follow serum lead levels. Allow minimum of 2 wk between courses unless blood levels require more aggressive management. Side effects: GI symptoms, increased LFTs (10%), rash, headaches, and dizziness. **Coadministration with other chelating agents is not recommended.** Treatment of iron deficiency is recommended, as well as environmental remediation. Contents of capsule may be sprinkled on food for those unable to swallow capsule.

**SUCCINYLCHOLINE**

Anectine, Quelicin, Quelicin-1000

**Neuromuscular blocking agent**

Yes



No



?



C

**Injection:**

Anectine, Quelicin: 20 mg/mL (10 mL); contains parabens

Quelicin-1000: 100 mg/mL (10 mL); may contain parabens and/or benzyl alcohol

**Paralysis for intubation (see remarks):****Infant and child:****Initial:****IV:** 1–2 mg/kg/dose  $\times$  1**IM:** 2.5–4 mg/kg/dose  $\times$  1**Max. dose:** 150 mg/dose**Maintenance:** 0.3–0.6 mg/kg/dose IV Q5–10 min PRN. Continuous infusion **not recommended** owing to risk of malignant hyperthermia.**Adult:****Initial:****IV:** 0.3–1.1 mg/kg/dose  $\times$  1**IM:** 2.5–4 mg/kg/dose  $\times$  1**Max. dose:** 150 mg/dose**Maintenance:** 0.04–0.07 mg/kg/dose IV Q5–10 min PRN. Continuous infusion **not recommended**.

Pretreatment with atropine is recommended to reduce incidence of bradycardia. For rapid sequence intubation, see Chapter 1.

**Contraindicated** after acute phase of an injury after major burns, multiple trauma, extensive denervation of skeletal muscle, or upper motor neuron injury, because severe hyperkalemia and subsequent **cardiac arrest** may occur.

**Cardiac arrest** has been reported in children and adolescents, primarily those with skeletal muscle myopathies (e.g., Duchenne muscular dystrophy). Identify developmental delays suggestive of a myopathy before use. Predose creatine kinase may be useful for identifying patients at risk. Monitoring of ECG for peaked T waves may be useful in detecting early signs of this adverse effect.

May cause malignant hyperthermia (use dantrolene to treat), bradycardia, hypotension, arrhythmia, and hyperkalemia. Severe anaphylactic reactions have been reported; **use caution** if previous anaphylactic reaction to other neuromuscular blocking agents. **Use with caution** in patients with severe burns, paraplegia, or crush injuries and in patients with preexisting hyperkalemia. Beware of prolonged depression in patients with liver disease, malnutrition, pseudocholinesterase deficiency, hypothermia, and those receiving aminoglycosides, phenothiazines, quinidine,  $\beta$ -blockers, amphotericin B, cyclophosphamide, diuretics, lithium, acetylcholine, and anticholinesterases. Diazepam may decrease neuromuscular blocking effects. Prior use of succinylcholine may enhance neuromuscular blocking effect of vecuronium and its duration of action.

Duration of action 4–6 min IV, 10–30 min IM. Must be prepared to intubate within 1 min.

**SUCRALFATE**

Carafate and many generics

**Oral antiulcer agent**

No



Yes



1



B

**Tabs:** 1 g**Oral suspension:** 100 mg/mL (420 mL); contains sorbitol and parabens**Child:****Duodenal or gastric ulcer:** 40–80 mg/kg/24 hr ÷ Q6 hr PO**Stomatitis:** 5–10 mL (500–1000 mg of suspension), swish and spit or swish and swallow QID**Adult:****Duodenal ulcer:****Treatment:** 1 g PO QID (1 hr before meals and QHS) or 2 g PO BID × 4–8 wk**Maintenance/prophylaxis:** 1 g PO BID**Stress ulcer:****Treatment:** 1 g PO Q4 hr**Prophylaxis:** 1 g PO QID**Stomatitis:** 10 mL (1000 mg of suspension), swish and spit or swish and swallow QID**Proctitis (use oral suspension as rectal enema):** 20 mL (2 g) PR once daily–BID

May cause vertigo, constipation, and dry mouth. Hypersensitivity, including anaphylactic reaction, has been reported. Hyperglycemia has been reported in diabetic patients. Aluminum may accumulate in patients with renal failure. This may be augmented by the use of aluminum-containing antacids. **Use with caution** in patients with dysphagia or other conditions that may alter gag or cough reflexes or diminish oropharyngeal coordination/motility in those receiving the oral tablet dosage form; cases of tablet aspiration with respiratory complications have been reported.

Decreases absorption of phenytoin, digoxin, theophylline, cimetidine, fat-soluble vitamins, ketoconazole, omeprazole, quinolones, and oral anticoagulants. Administer these drugs at least 2 hr before or after sucralfate doses.

Drug requires an acidic environment to form a protective polymer coating for damaged GI tract mucosa. Administer oral doses on an empty stomach (1 hr before meals and QHS).

**SULFACETAMIDE SODIUM OPHTHALMIC**

Bleph-10 and various generics

**Ophthalmic antibiotic, sulfonamide derivative**

No



No



?



C

**Ophthalmic solution:** 10% (5, 15 mL); may contain methylparaben and propylparaben**Ophthalmic ointment:** 10% (3.5 g); may contain phenylmercuric acetate**Ophthalmic (usual duration of therapy for ophthalmic use is 7–10 days):****>2 mo and adult:****Ointment:** Apply 0.5-inch ribbon into conjunctival sac Q3–4 hr and QHS initially, and reduce the dosing frequency with adequate response.**Drops:** 1–2 drops to affected eye(s) Q2–3 hr initially, and reduce the dosing frequency with adequate response.

Hypersensitivity reactions between different sulfonamides can occur regardless of route of administration. May cause local irritation, stinging, burning, conjunctival hyperemia, excessive tear production, and eye pain. Rare toxic epidermal necrolysis and Stevens-Johnson syndrome have been reported. Sulfacetamide preparations are incompatible with silver preparations.

To reduce risk of systemic absorption with ophthalmic solution, apply finger pressure to lacrimal sac during and 1–2 min after instillation.

**SULFADIAZINE**

Various generic products

**Antibiotic, sulfonamide derivative**

Yes




Yes



3



C/D

**Tabs:** 500 mg**Oral suspension:** 100, 200 mg/mL **Infant  $\geq$  2 mo, child, and adolescent:** 75 mg/kg/dose or 2000 mg/m<sup>2</sup>/dose PO  $\times$  1, followed by 150 mg/kg/24 hr or 4000 mg/m<sup>2</sup>/24 hr  $\div$  Q4–6 hr (**max. dose:** 6000 mg/24 hr).**Adult:** 2–4 g/dose  $\times$  1, followed by 2–4 g/24 hr PO  $\div$  Q4–8 hr**Congenital toxoplasmosis (administer with pyrimethamine and folinic acid; see pyrimethamine for dosage information):****Infant:** 100 mg/kg/24 hr PO  $\div$  BID  $\times$  12 mo**Toxoplasmosis (administer with pyrimethamine and folinic acid; see pyrimethamine for dosage information):****Infant  $\geq$  2 mo and child:** 100–200 mg/kg/24 hr  $\div$  Q6 hr PO  $\times$  3–4 wk; **max. dose:** 6000 mg/24 hr.**Adult:** 4–6 g/24 hr PO  $\div$  Q6 hr  $\times$  3–4 wk**Rheumatic fever prophylaxis:** **$\leq$  27 kg:** 500 mg PO once daily **$>$  27 kg:** 1000 mg PO once daily

Most cases of acquired toxoplasmosis do not require specific antimicrobial therapy.

**Contraindicated** in porphyria and hypersensitivity to sulfonamides. **Use with caution** in premature infants and infants  $<$  2 mo because of risk of hyperbilirubinemia, and in hepatic or renal dysfunction (30%–44% eliminated in urine). Maintain hydration. May cause fever, rash, hepatitis, SLE-like syndrome, vasculitis, bone marrow suppression, and hemolysis in patients with G6PD deficiency, and Stevens-Johnson syndrome.

May cause increased effects of warfarin, methotrexate, thiazide diuretics, uricosuric agents, and sulfonylureas owing to drug displacement from protein-binding sites. Large quantities of vitamin C or acidifying agents (e.g., cranberry juice) may cause crystalluria. Pregnancy category changes from "C" to "D" if administered near term. Administer on an empty stomach with plenty of water.

**SULFAMETHOXAZOLE AND TRIMETHOPRIM**

Trimethoprim-sulfamethoxazole, Co-Trimoxazole, TMP-SMX;

Bactrim, Septra, Sulfatrim, and others

**Antibiotic, sulfonamide derivative**

Yes



Yes



2



D

**Tabs (regular strength):** 80 mg TMP/400 mg SMX**Tabs (double strength):** 160 mg TMP/800 mg SMX**Oral suspension:** 40 mg TMP/200 mg SMX per 5 mL (100, 480 mL)**Injection:** 16 mg TMP/mL and 80 mg SMX/mL (5, 10, 30 mL); some preparations may contain propylene glycol and benzyl alcohol.**Doses based on TMP component.****Minor/moderate infections (PO or IV):****Child:** 8–12 mg/kg/24 hr  $\div$  BID**Adult ( $>$  40 kg):** 160 mg/dose BID**Severe infections (PO or IV):****Child and adult:** 20 mg/kg/24 hr  $\div$  Q6–8 hr**UTI prophylaxis:****Child:** 2–4 mg/kg/24 hr PO once daily

Continued

SULFAMETHOXAZOLE AND TRIMETHOPRIM *continued****Pneumocystis jirovecii (carinii) pneumonia (PCP):*****Treatment (PO or IV):** 20 mg/kg/24 hr ÷ Q6–8 hr × 21 days***Prophylaxis (PO or IV):***≥ 1 mo and child: 150 mg/m<sup>2</sup>/24 hr ÷ BID for 3 consecutive days/wk; **max. dose:** 320 mg/24 hr**Adult:** 160 mg once daily or 160 mg 3 days/wk

**Not recommended** for use with infants <2 mo (excluding PCP prophylaxis). **Contraindicated** in patients with sulfonamide or trimethoprim hypersensitivity, and megaloblastic anemia due to folate deficiency. May cause kernicterus in newborns. May cause blood dyscrasias, crystalluria, glossitis, renal or hepatic injury, GI irritation, rash, Stevens-Johnson syndrome, hemolysis in patients with G6PD deficiency. Severe hyponatremia may occur during treatment of PCP. Hyperkalemia may appear in HIV/AIDS patients. **Use with caution** in renal and hepatic impairment and G6PD deficiency. QT prolongation resulting in ventricular tachycardia has been reported.

Epidemiologic studies suggest use during pregnancy may be associated with increase risk of congenital malformations (particularly neural tube defects), cardiovascular malformations, urinary tract defects, oral clefts, and club foot.

Sulfamethoxazole is a CYP 450 2C9 substrate and inhibitor. Trimethoprim is a CYP 450 2C9, 3A4 substrate and 2C8/9 inhibitor. **Reduce dose in renal impairment (see Chapter 31). See Chapter 17 for PCP prophylaxis guidelines.**

**SULFASALAZINE**

Sulfazine, Sulfazine EC, Azulfidine, Azulfidine EN-tabs, Salicylazosulfapyridine and generics

***Antiinflammatory agent***

Yes



Yes



2



B/D

**Tabs:** 500 mg**Delayed-release tabs (Azulfidine EN-tabs, Sulfazine EC):** 500 mg**Oral suspension:** 100 mg/mL ***Inflammatory bowel disease:******Child ≥ 6 yr:******Initial dosing:*****Mild:** 40–50 mg/kg/24 hr ÷ Q6 hr PO**Moderate/severe:** 50–75 mg/kg/24 hr ÷ Q4–6 hr PO**Max. initial dose:** 4 g/24 hr**Maintenance:** 30–70 mg/kg/24 hr ÷ Q4–8 hr PO; **max. dose:** 4 g/24 hr***Adult:*****Initial:** 3–4 g/24 hr ÷ Q4–8 hr PO**Maintenance:** 2 g/24 hr ÷ Q6 hr PO**Max. dose:** 6 g/24 hr***Juvenile idiopathic arthritis:***

**Child 6–16 yr:** Start with 10 mg/kg/24 hr ÷ BID PO, and increase by 10 mg/kg/24 hr Q7 days until planned maintenance dose is achieved. Usual maintenance dose is 30–50 mg/kg/24 hr ÷ BID PO up to a **max.** of 2 g/24 hr.

**Contraindicated** in sulfa or salicylate hypersensitivity, porphyria, and GI or GU obstruction. **Use with caution** in renal impairment, blood dyscrasias, or asthma. Maintain hydration. May cause orange-yellow discoloration of urine and skin. May permanently stain contact lenses.

SULFASALAZINE *continued*

May cause photosensitivity, hypersensitivity, blood dyscrasias, CNS changes, nausea, vomiting, anorexia, diarrhea, and renal damage. Hepatotoxicity/hepatic failure, anaphylaxis, angioedema, severe drug rash with eosinophilia and systemic symptoms (DRESS), interstitial lung disease have been reported. May cause hemolysis in patients with G6PD deficiency. Decreases folic acid absorption and reduces serum digoxin and cyclosporine levels. Slow acetylators may require lower dosage owing to accumulation of active sulfapyridine metabolite.

Pregnancy category changes to "D" if administered near term. Bloody stools or diarrhea have been reported in breast-fed infants of mothers receiving sulfasalazine.

**SUMATRIPTAN SUCCINATE**

Imitrex, Alsuma, and generics

**Antimigraine agent, selective serotonin agonist**



Yes



Yes




2



C

**Injection for subcutaneous use:** 8, 12 mg/mL (0.5 mL)

**Tabs:** 25, 50, 100 mg

**Oral suspension:** 5 mg/mL 

**Nasal spray (as a unit-dose spray device):** 5 mg dose in 100 microliters (6 units per pack); 20 mg dose in 100 microliters (6 units per pack)

**Adolescent and adult (see remarks):**

**PO:** 25 mg as soon as possible after onset of headache. If no relief in 2 hr, give 25–100 mg Q2 hr up to a daily **max.** of 200 mg.

**Max. single dose:** 100 mg/dose

**Max. daily dose:** 200 mg/24 hr (with exclusive PO dosing or with an initial SC dose and subsequent PO dosing)

**SC:** 4–6 mg  $\times$  1 as soon as possible after onset of headache. If no response, may give an additional dose 1 hr later; **max. daily dose:** 12 mg/24 hr.

**Nasal:** 5–20 mg/dose into one nostril or divided into each nostril after onset of headache. Dose may be repeated in 2 hr up to a **max.** of 40 mg/24 hr.

**Contraindicated** with concomitant administration of ergotamine derivatives, MAOIs (and use within the past 2 wk) or other vasoconstrictive drugs. **Not** for migraine prophylaxis. **Use with caution** in renal or hepatic impairment. **A max. single dose** of 50 mg has been recommended in adults with hepatic dysfunction. Acts as selective agonist for serotonin receptor. Induration and swelling at injection site, flushing, dizziness, chest, jaw and neck tightness may occur with SC administration. Weakness, hyperreflexia, incoordination, and serotonin syndrome (may be life threatening) have been reported with use in combination with SSRIs (e.g., fluoxetine, fluvoxamine, paroxetine, sertraline).

May cause coronary vasospasm if administered IV. **Use injectable form SC only!** Onset of action is 10–120 min SC and 60–90 min PO. For nasal use, the safety of treating more than 4 headaches in a 30-day period has not been established.

Efficacy studies were not conclusive in clinical trials for children. Some **do not recommend** use in patients <18 yr owing to poor efficacy and reports of serious adverse events (e.g., stroke, visual loss, death) in both children and adults with all dosage forms.

To minimize infant exposure to sumatriptan, avoid breast-feeding for 12 hr after treatment.



**SURFACTANT, PULMONARY/BERACTANT**

Survanta

*Bovine lung surfactant*

**Suspension for inhalation:** 25 mg/mL phospholipids (4, 8 mL); contains 0.5–1.75 mg triglycerides, 1.4–3.5 mg free fatty acids, and <1 mg protein per 1 mL drug

**Prophylactic therapy:** 4 mL/kg/dose intratracheally as soon as possible. Up to 4 doses may be given at intervals no shorter than Q6 hr during first 48 hr of life.

**Rescue therapy (treatment):** 4 mL/kg/dose intratracheally, immediately after diagnosis of respiratory distress syndrome (RDS). May repeat dose as needed Q6 hr to **max.** of 4 doses total.

**Method of administration for previously listed therapies (see remarks):** Suction infant before administration. Each dose is divided into 4 1-mL/kg aliquots; administer 1 mL/kg in each of 4 different positions (slight downward inclination with head turned to right, head turned to left; slight upward inclination with head turned to right, head turned to left).

Transient bradycardia, O<sub>2</sub> desaturation, pallor, vasoconstriction, hypotension, endotracheal tube blockage, hypercarbia, hypercapnia, apnea, and hypertension may occur during administration process. Other side effects may include pulmonary interstitial emphysema, pulmonary air leak, and posttreatment nosocomial sepsis. Monitor heart rate and transcutaneous O<sub>2</sub> saturation during dose administration. Monitor arterial blood gases for post-dose hyperoxia and hypocarbia after administration.

All doses are administered intratracheally via a 5 french feeding catheter. If suspension settles during storage, gently swirl contents—**do not shake**. Drug is stored in refrigerator, protected from light, and has to be warmed by standing at room temperature for at least 20 min or warmed in the hand for at least 8 min. Artificial warming methods should **NOT** be used.

**SURFACTANT, PULMONARY/CALFACTANT**

Infasurf

*Bovine lung surfactant*

**Intratracheal suspension:** 35 mg/mL phospholipids (3, 6 mL); contains 26 mg phosphatidylcholine, 0.7 mg protein, and 0.26 mg surfactant protein B per 1 mL

**Prophylactic therapy:** 3 mL/kg/dose intratracheally as soon as possible. Up to a total of 3 doses may be given Q12 hr.

**Rescue therapy (treatment [see remarks]):** 3 mL/kg/dose intratracheally immediately after diagnosis of respiratory distress syndrome (RDS). May repeat dose as needed Q12 hr to **max.** of 3 doses total.

**Method of administration for previously listed therapies (see remarks):** Suction infant before administration. Manufacturer recommends administration through a side-port adapter into endotracheal tube with two attendants (one to instill drug and another to monitor and position patient). Each dose is divided into 2 1.5-mL/kg aliquots; administer 1.5 mL/kg in each of 2 different positions (infant positioned with either right or left side dependent). Drug is administered while ventilation is continued over 20–30 breaths for each aliquot, with small bursts timed only during inspiratory cycles. A pause followed by evaluation of respiratory status and repositioning should separate the 2 aliquots. Drug has also been administered by divided dose into 4 equal aliquots and administered with repositioning in prone, supine, right, and left lateral positions.

Common adverse effects include cyanosis, airway obstruction, bradycardia, reflux of surfactant into ET tube, requirement for manual ventilation, and reintubation. Monitor O<sub>2</sub> saturation and lung compliance after each dose such that oxygen therapy and ventilator pressure are adjusted as necessary.

SURFACTANT, PULMONARY/CALFACTANT *continued*

All doses administered intratracheally via a 5 french feeding catheter. If suspension settles during storage, gently swirl contents—**do not shake**. Drug is stored in refrigerator, protected from light, and does not have to be warmed before administration. Unopened vials that have been warmed to room temperature (once only) may be refrigerated within 24 hours and stored for future use.

For rescue therapy, repeat doses may be administered as early as 6 hr after previous dose for a total of up to 4 doses if infant is still intubated and requires at least 30% inspired oxygen to maintain a  $P_{aO_2} \geq 80$  torr.

**SURFACTANT, PULMONARY/LUCINACTANT**

Surfaxin

**Synthetic lung surfactant**

No



No



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**Suspension for inhalation:** 30 mg/mL phospholipids (8.5 mL); contains 4.05 mg palmitic acid and 0.862 mg sinapultide per 1 mL drug

**Prophylaxis therapy:** 5.8 mL/kg/dose intratracheally as soon as possible; up to 4 doses may be given at intervals no shorter than 6 hr during first 48 hr of life.



**Method of administration (see remarks):** Suction infant before administration. Each dose is divided into 4 aliquots. Position infant in right lateral decubitus position with head and thorax inclined upward 30 degrees. Instill first aliquot (¼ of total dose) as a bolus while continuing positive-pressure mechanical ventilation and maintaining positive end-expiratory pressure of 4 to 5 cc  $H_2O$  (ventilator setting may be adjusted at clinician's discretion to maintain appropriate oxygenation and ventilation). Ventilate until infant is stable (at least 90%  $O_2$  saturation and heart rate  $\geq 120$  beats/min), and repeat procedure and administer 2nd aliquot with infant in left decubitus position while maintaining adequate positive-pressure ventilation. Administer 3rd and 4th aliquots by repeating aforementioned procedures with infant in right and then left decubitus position, respectively. Remove catheter after administering 4th aliquot, and resume ventilator management and care with infant's head elevated at least 10 degrees for at least 1–2 hr. **Do not** suction infant during first hour unless significant airway obstruction.

Currently FDA approved for prophylaxis (prevention) of RDS. Bradycardia, oxygen desaturation, reflux of drug into ET tube, and airway/ET tube obstruction may occur (drug administration should be interrupted if any of these events occur). Suctioning of ET tube or reintubation may be necessary if airway obstruction persists or is severe.



All doses administered intratracheally via a 5 french catheter. Warm each vial for 15 min in a preheated dry block heater set at 44°C. Then shake vial vigorously until contents is a uniform and free-flowing suspension. If not immediately used after warming, vial can be stored at room temperature and protected from light for up to 2 hr. **Do not** return vial to refrigerator after warming. Single-use vials; discard unused portion if not used within 2 hr of warming.

**SURFACTANT, PULMONARY/PORACTANT ALFA**

Curosurf

*Porcine lung surfactant*

No



No



?



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**Intratracheal suspension:** 80 mg/mL (1.5, 3 mL): contains 76 mg phospholipids, 1 mg and 0.45 mg surfactant protein B per 1 mL drug

**Rescue therapy (treatment):** 2.5 mL/kg/dose  $\times$  1 intratracheally immediately after diagnosis of respiratory distress syndrome (RDS). May administer 1.25 mL/kg/dose Q12 hr  $\times$  2 doses as needed up to a **max. total dose** of 5 mL/kg.



**Method of administration (see remarks):** Suction infant before administration. Each dose is divided into 2 aliquots, with each aliquot administered into 1 of the 2 main bronchi by positioning infant with either right or left side dependent. After first aliquot is administered, remove catheter from ET tube and manually ventilate infant with 100% oxygen at a rate of 40–60 breaths/min for 1 min. When infant is stable, reposition infant and administer second dose with same procedures. Then remove catheter **without** flushing.

Currently FDA approved for treatment (rescue therapy) of RDS. Transient episodes of bradycardia, decreased oxygen saturation, reflux of surfactant into ET tube, and airway obstruction have occurred during dose administration. Monitor O<sub>2</sub> saturation and lung compliance after each dose, and adjust oxygen therapy and ventilator pressure as necessary. Pulmonary hemorrhage has been reported.



All doses administered intratracheally via a 5 french feeding catheter. Suction infant before administration and 1 hr after surfactant instillation (unless signs of significant airway obstruction).

Drug is stored in refrigerator and protected from light. Each vial of drug should be slowly warmed to room temperature and gently turned upside down for uniform suspension (**do not shake**) before administration. Unopened vials that have been warmed to room temperature (once only) may be refrigerated within 24 hr and stored for future use.

**TACROLIMUS**

Astragraf XL, FK506, Hecoria, Prograf, Protopic, and generics

*Immunosuppressant*

Yes



Yes



2



C

**Caps (Hecoria, Prograf, and generics):** 0.5, 1, 5 mg

**Extended-release caps (Astragraf XL):** 0.5, 1, 5 mg (see remarks)

**Oral suspension:** 0.5, 1 mg/mL

**Injection (Prograf):** 5 mg/mL (1 mL); contains alcohol, and polyoxyl 60 hydrogenated castor oil (cremophor)

**Topical ointment (Protopic):** 0.03%, 0.1% (30, 60, 100 g)

**Child:**

**Liver transplantation without preexisting renal or hepatic dysfunction (initial doses; titrate to therapeutic levels):**

**IV:** 0.03–0.05 mg/kg/24 hr by continuous infusion

**PO:** 0.15–0.2 mg/kg/24 hr  $\div$  Q12 hr

**Adult (initial doses; titrate to therapeutic levels):**

**IV:** 0.01–0.05 mg/kg/24 hr by continuous infusion

**PO:** 0.075–0.2 mg/kg/24 hr  $\div$  Q12 hr

**Liver transplantation:** 0.1–0.15 mg/kg/24 hr  $\div$  Q12 hr

**Kidney transplantation:** 0.1–0.2 mg/kg/24 hr  $\div$  Q12 hr

**Cardiac transplantation:** 0.075 mg/kg/24 hr  $\div$  Q12 hr



TACROLIMUS *continued*

**Atopic dermatitis (continue treatment for 1 wk after clearing of signs and symptoms [see remarks]):**

**Child ≥ 2–15 yr old:** Apply a thin layer of 0.03% ointment to affected skin areas BID and rub in gently and completely.

**Adolescent ≥ 16 yr and adult:** Apply a thin layer of 0.03% or 0.1% ointment to affected skin areas BID and rub in gently and completely.

**Avoid** use in patients with prolonged cardiac QT intervals. IV dosage form **contraindicated** in patients allergic to polyoxyl 60 hydrogenated castor oil (cremophor). Experience in pediatric kidney transplantation is limited. Pediatric patients have required higher mg/kg doses than adults. For BMT use (beginning 1 day before BMT), dose and therapeutic levels similar to those in liver transplantation have been used.



Major adverse events include tremor, headache, insomnia, diarrhea, constipation, hypertension, nausea, and renal dysfunction. Hypokalemia, hypomagnesemia, hyperglycemia, confusion, depression, infections, lymphoma, liver enzyme elevation, and coagulation disorders may also occur. GI perforation, agranulocytosis, and hemolytic anemia have been reported.

Tacrolimus is a substrate of the CYP 450 3A4 drug metabolizing enzyme. Calcium channel blockers, imidazole antifungals (ketoconazole, itraconazole, fluconazole, clotrimazole, posaconazole), macrolide antibiotics (erythromycin, clarithromycin, troleandomycin), cisapride, cimetidine, cyclosporine, danazol, methylprednisolone, and grapefruit juice can increase tacrolimus serum levels. In contrast, carbamazepine, caspofungin, phenobarbital, phenytoin, rifampin, rifabutin, and sirolimus may decrease levels. Use with sirolimus may increase risk for hepatic artery thrombosis. Use with other CYP 450 3A inhibitors and substrates have the potential to prolong cardiac QT interval. Reduce dose in renal or hepatic insufficiency.

Monitor trough levels (just before a dose at steady state). Steady state is generally achieved after 2–5 days of continuous dosing. Interpretation will vary based on treatment protocol and assay methodology (whole blood ELISA vs. MEIA vs. HPLC). Whole blood trough concentrations of 5–20 ng/mL have been recommended in liver transplantation at 1–12 mo. Trough levels of 7–20 ng/mL (whole blood) for the first 3 mo and 5–15 ng/mL after 3 mo have been recommended in renal transplantation.

Tacrolimus therapy generally should be initiated 6 hr or more after transplantation. PO is the preferred route of administration and should be administered on an empty stomach. Safety and efficacy of extended-release capsules have not been established for kidney transplant patients <16 yr old. IV infusions should be administered at concentrations between 0.004 and 0.02 mg/mL diluted with NS or D<sub>5</sub>W.

**TOPICAL USE: Not recommended** for use in patients with skin conditions with a skin barrier defect with potential for systemic absorption. **Do not use** in children <2 yr, immunocompromised patients, or with occlusive dressings (promotes systemic absorption). Approved as second-line therapy for short-term and intermittent treatment of atopic dermatitis for patients who fail to respond or do not tolerate other approved therapies. Long-term safety is unknown. Skin burn sensation, pruritus, flulike symptoms, allergic reaction, skin erythema, headache, and skin infection are the most common side effects. Application site edema has been reported. Although the risk is uncertain, the FDA has issued an alert about potential cancer risk with use of this product. See [www.fda.gov/medwatch](http://www.fda.gov/medwatch) for latest information.

**TERBUTALINE**

Various generics; previously available as Brethine

 **$\beta_2$ -Adrenergic agonist**

No



Yes



?



C

Tabs: 2.5, 5 mg

Oral suspension: 1 mg/mL

Injection: 1 mg/mL (1 mL)

**Oral:**≤12 yr: **Initial:** 0.05 mg/kg/dose Q8 hr; increase as required; **max. dose:** 0.15 mg/kg/dose Q8 hr or total of 5 mg/24 hr

&gt;12 yr and adult: 2.5–5 mg/dose PO Q6–8 hr

**Max. dose:**

12–15 yr: 7.5 mg/24 hr

&gt;15 yr: 15 mg/24 hr

**Nebulization:**

&lt;2 yr: 0.5 mg in 2.5 mL NS Q4–6 hr PRN

2–9 yr: 1 mg in 2.5 mL NS Q4–6 hr PRN

&gt;9 yr: 1.5–2.5 mg in 2.5 mL NS Q4–6 hr PRN

**SC injection:**≤12 yr: 0.005–0.01 mg/kg/dose (**max. dose:** 0.4 mg/dose) Q15–20 min × 3; if needed, Q2–6 hr PRN>12 yr and adult: 0.25 mg/dose Q15–30 min PRN × 3; **max. total dose:** 0.75 mg**Continuous infusion, IV:** 2–10 mcg/kg loading dose, followed by infusion of 0.1–0.4 mcg/kg/min. May titrate in increments of 0.1–0.2 mcg/kg/min Q30 min depending on clinical response. Doses as high as 10 mcg/kg/min have been used. **To prepare infusion, see IV Infusions on page i.**

Use of IV and PO routes should **not** be used for prevention or prolonged treatment of preterm labor; potential for serious maternal **cardiac events and even death**. Nervousness, tremor, headache, nausea, tachycardia, arrhythmias, and palpitations may occur. Paradoxical bronchoconstriction may occur with excessive use; if it occurs, discontinue drug immediately. Injectable product may be used for nebulization. For acute asthma, nebulizations may be given more frequently than Q4–6 hr. Use spacer device with inhaler to optimize drug delivery.

Monitor heart rate, blood pressure, respiratory rate, and serum potassium when using continuous IV infusion route of administration. **Adjust dose in renal failure (see Chapter 31).**

**TETRACYCLINE HCL**

Various generics; previously available as Sumycin

**Antibiotic**

Yes



Yes



2



D

Caps: 250, 500 mg

Oral suspension: 25 mg/mL

**Do not use in children <8 yr.****Child ≥ 8 yr:** 25–50 mg/kg/24 hr PO ÷ Q6 hr; **max. dose:** 3 g/24 hr**Adult:** 1–2 g/24 hr PO ÷ Q6–12 hr**Acne vulgaris:** 250 mg PO every other day to 500 mg PO once daily

**Not recommended** in patients <8 yr, owing to tooth staining and decreased bone growth. Also **not recommended** for use in pregnancy, because these side effects may occur in the fetus. Risk for these adverse effects are highest with long-term use. May cause nausea, GI upset,

TETRACYCLINE HCL *continued*

hepatotoxicity, stomatitis, rash, fever, and superinfection. Photosensitivity reaction may occur. Avoid prolonged exposure to sunlight.

**Never use outdated tetracyclines;** they may cause Fanconi-like syndrome. **Do not** give with dairy products or any divalent cations (i.e.,  $\text{Fe}^{2+}$ ,  $\text{Ca}^{2+}$ ,  $\text{Mg}^{2+}$ ). Give 1 hr before or 2 hr after meals. May decrease effectiveness of oral contraceptives, increase serum digoxin levels, and increase effects of warfarin. Use with methoxyflurane increases risk for nephrotoxicity. Use with isotretinoin is associated with pseudotumor cerebri. **Adjust dose in renal failure (see Chapter 31).** Short-term maternal use is not likely to cause harm to breast-feeding infant.

**THEOPHYLLINE**

Theo-24, Theochron, Elixophyllin, and generics

**Bronchodilator, methylxanthine**



Yes



No



2



C

Other dosage forms may exist.

**Immediate release:**

Elixir (Elixophyllin): 80 mg/15 mL (473 mL); may contain up to 20% alcohol

**Sustained/extended release (see remarks):****Tabs:**

**Q12 hr dosing, Theochron and generics:** 100, 200, 300, 450 mg

**Q24 hr dosing, generics:** 400, 600 mg

**Caps (Q24 hr dosing: Theo-24):** 100, 200, 300, 400 mg

Sustained-release forms should **not** be chewed or crushed. Capsules may be opened and contents sprinkled on food.

**Dosing intervals are for immediate-release preparations.**

For sustained-release preparations, divide daily dose >Q8–24 hr based on product.

**Neonatal apnea:**

**Loading dose:** 5 mg/kg/dose PO  $\times$  1

**Maintenance:** 3–6 mg/kg/24 hr PO  $\div$  Q6–8 hr

**Bronchospasm; PO:**

**Loading dose:** 1 mg/kg/dose for each 2 mg/L desired increase in serum theophylline level

**Maintenance, infant (<1 yr):**

**Preterm:**

**<24 days old (postnatal):** 1 mg/kg/dose PO Q12 hr

**$\geq$ 24 days old (postnatal):** 1.5 mg/kg/dose PO Q12 hr

**Full term up to 1 yr old:** Total daily dose (mg) =  $[(0.2 \times \text{age in weeks}) + 5] \times (\text{kg body weight})$

**$\leq$ 6 mo:** Divide daily dose Q8 hr.

**>6 mo:** Divide daily dose Q6 hr.

**Maintenance, child > 1 yr and adult without risk factors for altered clearance (see remarks):**

**<45 kg:** Begin therapy at 12–14 mg/kg/24 hr  $\div$  Q4–6 hr up to **max. dose** of 300 mg/24 hr. If needed (based on serum levels), gradually increase to 16–20 mg/kg/24 hr  $\div$  Q4–6 hr. **Max. dose:** 600 mg/24 hr.

**$\geq$ 45 kg:** Begin therapy with 300 mg/24 hr  $\div$  Q6–8 hr. If needed (based on serum levels), gradually increase to 400–600 mg/24 hr  $\div$  Q6–8 hr.

Drug metabolism varies widely with age, drug formulation, and route of administration. Most common side effects and toxicities are nausea, vomiting, anorexia, abdominal pain, gastroesophageal reflux, nervousness, tachycardia, seizures, and arrhythmias.



*Continued*

THEOPHYLLINE *continued*

Serum levels should be monitored. Therapeutic levels: bronchospasm, 10–20 mg/L; apnea, 7–13 mg/L. Half-life is age dependent: 30 hr (newborns); 6.9 hr (infants); 3.4 hr (children); 8.1 hr (adults). See *Aminophylline* for guidelines for serum level determinations. Liver impairment, cardiac failure, and sustained high fever may increase theophylline levels. Theophylline is a substrate for CYP 450 1A2. Levels are increased with allopurinol, alcohol, ciprofloxacin, cimetidine, clarithromycin, disulfiram, erythromycin, estrogen, isoniazid, propranolol, thiabendazole, and verapamil. Levels are decreased with carbamazepine, isoproterenol, phenobarbital, phenytoin, and rifampin. May cause increased skeletal muscle activity, agitation, and hyperactivity when used with doxapram. May increase quinine levels/toxicity.

Because of poor distribution into body fat, use ideal body weight in obese patients when calculating dosage. Risk factors for increased clearance include smoking, cystic fibrosis, hyperthyroidism, and high-protein diet. Factors for decreased clearance include CHF, correction of hyperthyroidism, fever, viral illness, sepsis and high carbohydrate diet.

Suggested dosage intervals for sustained-released products (see following table):

**Theophylline Sustained-Release Products**

Trade Name	Available Strengths	Dosage Interval
<b>CAPSULES</b>		
Theo-24	100, 200, 300, 400 mg	Q24 hr
<b>TABLETS</b>		
Theocron	100, 200, 300, 450 mg	Q12–24 hr
Generic	400, 600 mg	Q24 hr

**THIAMINE**

Vitamin B<sub>1</sub>, many generic products

**Water-soluble vitamin**



No



No



1



A/C

**Tabs [OTC]:** 50, 100, 250, 500 mg

**Caps [OTC]:** 50, 100, 500 mg

**Injection:** 100 mg/mL (2 mL); may contain benzyl alcohol

For US RDA, see Chapter 21.

**Beriberi (thiamine deficiency):**

**Child:** 10–25 mg/dose IM/IV once daily (if critically ill) *OR* 10–50 mg/dose PO once daily × 2 wk, followed by 5–10 mg/dose once daily × 1 mo

**Adult:** 5–30 mg/dose IM/IV TID (if critically ill) × 2 wk, followed by 5–30 mg/24 hr PO ÷ once daily or TID × 1 mo

**Wernicke's encephalopathy syndrome:**

**Adult:** 100 mg IV × 1, then 50–100 mg IM/IV once daily until patient resumes a normal diet. (Administer thiamine before starting glucose infusion.)

Multivitamin preparations contain amounts meeting RDA requirements. Allergic reactions and anaphylaxis may occur, primarily with IV administration. Therapeutic range: 1.6–4 mg/dL. High-carbohydrate diets or IV dextrose solutions may increase thiamine requirements. Large doses may interfere with serum theophylline assay. Pregnancy category changes to "C" if used in doses above the RDA.



**THIORIDAZINE**

Various generic products, previously available as Mellaril  
**Antipsychotic, phenothiazine derivative**



Yes



No



?



C

**Tabs:** 10, 25, 50, 100 mg

**Child 2–12 yr:** Start with 0.5 mg/kg/24 hr PO ÷ BID–TID; dosage range: 0.5–3 mg/kg/24 hr PO ÷ BID–TID. **Max. dose:** 3 mg/kg/24 hr.

**>12 yr and adult:** Start with 75–300 mg/24 hr PO ÷ TID. Then gradually increase PRN to **max. dose** of 800 mg/24 hr ÷ BID–QID.



Indicated for schizophrenia unresponsive to standard therapy. **Contraindicated** in severe CNS depression, brain damage, narrow-angle glaucoma, blood dyscrasias, and severe liver or cardiovascular disease. **DO NOT** coadminister with drugs that may inhibit CYP 450 2D6 isoenzymes (e.g., SSRIs [fluoxetine, fluvoxamine, paroxetine],  $\beta$ -blockers [propranolol, pindolol], drugs that may widen QTc interval (e.g., disopyramide, procainamide, quinidine), or in patients with known reduced activity of CYP 450 2D6.



May cause drowsiness, extrapyramidal reactions, autonomic symptoms, ECG changes (QTc prolongation in a dose-dependent manner), arrhythmias, paradoxical reactions, and endocrine disturbances. Long-term use may cause tardive dyskinesia. Pigmentary retinopathy may occur with higher doses; a periodic eye examination is recommended. More autonomic symptoms and less extrapyramidal effects than chlorpromazine. Concurrent use with epinephrine can cause hypotension. Increased cardiac arrhythmias may occur with tricyclic antidepressants.

In an overdose situation, monitor ECG and avoid drugs that can widen QTc interval.

**TIAGABINE**

Gabitril and generics  
**Anticonvulsant**



Yes



No



?



C

**Tabs:** 2, 4, 12, 16 mg

**Oral suspension:** 1 mg/mL

**Adjunctive therapy for refractory seizures (see remarks):**



**Child  $\geq 2$  yr (limited data from a safety and tolerability study in 52 children 2–17 yr,**

**mean  $9.3 \pm 4.1$ ):** Initial dose of 0.25 mg/kg/24 hr PO ÷ TID  $\times$  4 wk. Dosage was increased at 4-wk intervals to 0.5, 1, and 1.5 mg/kg/24 hr until an effective and well-tolerated dose was established. Criteria for dose increase required tolerance of the current dosage level and  $<50\%$  reduction in seizures. Patients receiving enzyme-inducing antiepileptic drugs (AEDs) received a **max. daily dose** of  $0.73 \pm 0.44$  mg/kg/24 hr, and patients receiving non-enzyme-inducing AEDs received a **max.** of  $0.61 \pm 0.32$  mg/kg/24 hr.

**Adjunctive therapy for partial seizures (dosage based on use with enzyme-inducing AEDs (see remarks)):**

**$\geq 12$  yr and adult:** Start at 4 mg PO once daily  $\times$  7 days. If needed, increase dose to 8 mg/24 hr PO ÷ BID. Dosage may be increased further by 4–8 mg/24 hr at weekly intervals (daily doses may be divided BID–QID) until a clinical response is achieved or up to specified max. dose. **NOTE:** Patients receiving non-enzyme-inducing AEDs had tiagabine blood levels about 2 times higher than patients receiving enzyme-inducing AEDs.

**Max. dose:**

**12–18 yr:** 32 mg/24 hr

**Adult:** 56 mg/24 hr

Continued



TETRACYCLINE HCL *continued*

**Use with caution** in hepatic insufficiency (may have to reduce dose and/or increase dosing interval). Most common side effects include dizziness, somnolence, depression, confusion, and asthenia. Nervousness, tremor, nausea, abdominal pain, confusion, and difficulty in concentrating may also occur. Cognitive/neuropsychiatric symptoms resulting in nonconvulsive status epilepticus requiring subsequent dose reduction or drug discontinuation have been reported. Suicidal behavior or ideation has been reported. **Off-label use in patients WITHOUT epilepsy is discouraged** because of reports of seizures in these patients.

Tiagabine's clearance is increased by concurrent hepatic enzyme-inducing AEDs (e.g., phenytoin, carbamazepine, barbiturates). Lower doses or a slower titration for clinical response may be necessary for patients receiving non-enzyme-inducing drugs (e.g., valproate, gabapentin, lamotrigine). **Avoid** abrupt discontinuation of drug.

TID dosing schedule may be preferred because BID schedule may not be well tolerated. Doses should be administered with food.

**TICARCILLIN AND CLAVULANATE**

Timentin

**Antibiotic, penicillin (extended spectrum with  $\beta$ -lactamase inhibitor)**



Yes



Yes



2



B

**Injection:** 3.1 g (3 g ticarcillin and 0.1 g clavulanate); contains 4.51 mEq Na<sup>+</sup> and 0.15 mEq K<sup>+</sup> per 1 g drug

**Premixed injection:** 3.1 g (3 g ticarcillin and 0.1 g clavulanate) in 100 mL; contains 18.7 mEq Na<sup>+</sup> and 0.5 mEq K<sup>+</sup> per 100 mL

**All doses based on ticarcillin component.**

**Neonate (IV):**

**≤ 7 days:**

**< 2 kg:** 150 mg/kg/24 hr ÷ Q12 hr

**≥ 2 kg:** 225 mg/kg/24 hr ÷ Q8 hr

**> 7 days:**

**< 1.2 kg:** 150 mg/kg/24 hr ÷ Q12 hr

**1.2–2 kg:** 225 mg/kg/24 hr ÷ Q8 hr

**> 2 kg:** 300 mg/kg/24 hr ÷ Q8 hr

**Term neonate and infant < 3 mo:** 200–300 mg/kg/24 hr IV ÷ Q4–6 hr

**Infant ≥ 3 mo and child < 60 kg:**

**Mild/moderate infections:** 200 mg/kg/24 hr IV ÷ Q6 hr

**Severe infections:** 300 mg/kg/24 hr IV ÷ Q4–6 hr

**Max. dose:** 18–24 mg/24 hr

**Cystic fibrosis:** 300–600 mg/kg/24 hr IV ÷ Q4–6 hr IV. **Max. dose:** 24 g/24 hr.

**Adult:** 3 g/dose IV Q4–6 hr IV

**UTI:** 3 g/dose IV Q6–8 hr

**Max. dose:** 18–24 g/24 hr



$\beta$ -Lactamase inhibitor broadens spectrum to include *Staphylococcus aureus* and *Haemophilus influenzae*. Thrombophlebitis, rash, and immune hypersensitivity are common side effects. May also cause decreased platelet aggregation, bleeding diathesis, hypernatremia, hematuria, hypokalemia, hypocalcemia, allergy, and increased AST. Hemorrhagic cystitis has been reported. Use with caution with cephalosporin hypersensitivity and CHF (high sodium content). Like other penicillins, CSF penetration occurs only with inflamed meninges. May cause false-positive tests for urine protein and serum Coombs test.

Do not mix with aminoglycoside in same solution. Ticarcillin elimination is prolonged with impaired hepatic and/or renal function (**adjust dosage in renal impairment; see Chapter 31**).



**TOBRAMYCIN**

Bethkis, Nebcin, Tobrex, AKTob, TOBI, TOBI Podhaler, and generics

**Antibiotic, aminoglycoside**

No



Yes



2



B/D

**Injection:** 10, 40 mg/mL; may contain phenol and bisulfites**Premixed injection:** 80 mg in 100 mL NS**Powder for injection:** 1.2 g; preservative free**Ophthalmic ointment (Tobrex, AKTob):** 0.3% (3.5 g)**In combination with dexamethasone (TobraDex):** 0.3% tobramycin with 0.1% dexamethasone (3.5 g); contains 0.5% chlorbutanol**Ophthalmic solution (Tobrex):** 0.3% (5 mL)**In combination with dexamethasone:** 0.3% tobramycin with 0.1% dexamethasone (2.5, 5, 10 mL); contains 0.01% benzalkonium chloride and EDTA**Nebulizer solution:****Bethkis:** 300 mg/4 mL (56s); preservative free**TOBI and generic:** 300 mg/5 mL (56s); preservative free 170 mg/3.4 mL (mixed in 0.45% NS, preservative free, use with eFlow/Trio nebulizer) **Powder for inhalation:****TOBI Podhaler:** 28 mg capsules (224 capsules in 4 weekly packs with inhalation device)**Initial empirical dosage; patient-specific dosage defined by therapeutic drug monitoring (see remarks):****Neonate/infant, IM/IV (see following table):**

Postconceptional Age (wk)	Postnatal Age (Days)	Dose (mg/kg/dose)	Interval (hr)
≤29*	0–7	5	48
	8–28	4	36
	>28	4	24
30–33	0–7	4.5	36
	>7	4	24
34–37	0–7	4	24
	>7	4	18–24
≥38	0–7	4	24†
	>7	4	12–18

\*Or significant asphyxia, PDA, indomethacin use, poor cardiac output, reduced renal function.

†Use Q36 hr interval for HIE patients receiving whole-body therapeutic cooling.

**Child:** 7.5 mg/kg/24 hr ÷ Q8 hr IV/IM**Cystic fibrosis (if available, use patient's previous therapeutic mg/kg dosage):****Conventional Q8 hr dosing:** 7.5–10.5 mg/kg/24 hr ÷ Q8 hr IV**High-dose extended interval (once daily) dosing:** 10–12 mg/kg/dose Q24 hr IV**Adult:** 3–6 mg/kg/24 hr ÷ Q8 hr IV/IM**Ophthalmic:****Tobramycin:****Child and adult:****Ophthalmic ointment:** Apply 0.5-inch ribbon into conjunctival sac(s) BID–TID; for severe infections, apply Q3–4 hr.**Ophthalmic drop:** Instill 1–2 drops of solution to affected eye(s) Q4 hr; for severe infections, instill 2 drops Q30–60 min initially, then reduce dosing frequency.**Tobramycin with dexamethasone:**

Continued

TOBRAMYCIN *continued***≥2 yr and adult:**

**Ophthalmic ointment:** Apply 0.5-inch ribbon of ointment into conjunctival sac(s) TID–QID.

**Ophthalmic drop:** Instill 1–2 drops of solution to affected eye(s) Q2 hr × 24–48 hr, then 1–2 drops Q4–6 hr.

**Inhalation:****Cystic fibrosis prophylaxis therapy:****≥6 yr and adult:**

**Bethkis, TOBI, and generic product:** 300 mg Q12 hr administered in repeated cycles of 28 days on drug, followed by 28 days off drug.

**Use with eFlow/Trio nebulizer:** 170 mg Q12 hr administered in repeated cycles of 28 days on drug, followed by 28 days off drug.

**TOBI Podhaler:** Four 28-mg capsules Q12 hr administered in repeated cycles of 28 days on drug, followed by 28 days off drug.

**Use with caution** in combination with neurotoxic, ototoxic, or nephrotoxic drugs; anesthetics or neuromuscular blocking agents; preexisting renal, vestibular, or auditory impairment; and in patients with neuromuscular disorders. May cause ototoxicity, nephrotoxicity, and neuromuscular blockade. Serious allergic reactions including anaphylaxis, and dermatologic reactions, including exfoliative dermatitis, toxic epidermal necrolysis, erythema multiforme, and Stevens-Johnson syndrome have been reported rarely. **Ototoxic effects synergistic with furosemide.**



Higher doses are recommended in patients with cystic fibrosis, neutropenia, or burns. **Adjust dose in renal failure (see Chapter 31).** Monitor peak and trough levels.

**Therapeutic peak levels with conventional Q8 hr dosing:**

6–10 mg/L in general

8–10 mg/L in pulmonary infections, neutropenia, osteomyelitis, and severe sepsis

**Therapeutic trough levels with conventional Q8 hr dosing:** <2 mg/L. Recommended serum sampling time at steady state: trough within 30 min before third consecutive dose and peak 30–60 min after administration of third consecutive dose.

**Therapeutic peak and trough goals for high-dose extended-interval dosing for cystic fibrosis:**

**Peak:** 20–40 mg/L; recommended serum sampling time at 30–60 min after administration of first dose

**Trough:** <1 mg/L; recommended serum sampling time within 30 min before second dose

Serum levels should be rechecked with changing renal function, poor clinical response, and at a minimum of once weekly for prolonged therapies.

To maximize bactericidal effects, an individualized peak concentration to target a peak/MIC ratio of 8–10:1 may be applied.

For initial dosing in obese patients, use an adjusted body weight (ABW).  $ABW = \text{Ideal body weight} + 0.4 (\text{Total body weight} - \text{Ideal body weight})$ .

**INHALATIONAL USE:** Transient voice alteration, bronchospasm, dyspnea, pharyngitis, and increased cough may occur. Transient tinnitus and hearing loss have been reported. If used with other medications in cystic fibrosis, use the following order of administration: bronchodilator first, chest physiotherapy, other inhaled medications (if indicated), and tobramycin last. For TOBI Podhaler, inhale entire contents of each capsule.

Pregnancy category is "D" for injection and inhalation routes of administration and "B" for ophthalmic route.

**TOLNAFTATE**

Tinactin and many generics

**Antifungal agent**

No



No



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**Topical aerosol liquid [OTC]:** 1% (128, 150 g); may contain 29% vol/vol or 41% wt/wt alcohol**Aerosol powder [OTC]:** 1% (133 g); contains 11% vol/vol alcohol and talc**Cream [OTC]:** 1% (15, 30, 114 g)**Topical powder [OTC]:** 1% (45, 60, 108 g)**Topical solution [OTC]:** 1% (10, 30 mL)**Child ( $\geq 2$  yr) and adult:****Topical:** Apply 1–3 drops of solution or small amount of liquid, cream, or powder to affected areas BID–TID for 2–4 wk.May cause mild irritation and sensitivity. Contact dermatitis has been reported. **Avoid** eye contact. **Do not use** for nail or scalp infections. Discontinue use if sensitization develops.

Pregnancy category not formally assigned by FDA.

**TOPIRAMATE**

Topamax, Topiragen, Trokendi XR, and generics

**Anticonvulsant**

Yes



Yes



2



D

**Caps, sprinkle:** 15, 25 mg**Tabts:** 25, 50, 100, 200 mg**Extended-release caps (Trokendi XR; Q24 hr dosing):** 25, 50, 100, 200 mg**Oral suspension:** 6 mg/mL **Adjunctive therapy for partial onset seizures or Lennox-Gastaut syndrome:****Child 2–16 yr:** Start with 1–3 mg/kg/dose (**max. dose:** 25 mg/dose) PO QHS  $\times$  7 days, then increase by 1–3 mg/kg/24-hr increments at 1- to 2-wk intervals (divided daily dose BID) to response. Usual maintenance dose is 5–9 mg/kg/24 hr PO  $\div$  BID. **$\geq 17$  yr and adult:** Start with 25–50 mg PO QHS  $\times$  7 days, then increase by 25–50 mg/24 hr increments at 1-wk intervals until adequate response. Doses  $>50$  mg should be divided BID. Usual maintenance dose: 100–200 mg/24 hr. Doses above 1600 mg/24 hr have not been studied.**Adjunctive therapy for primary generalized tonic-clonic seizures:****Child 2–16 yr:** Use above initial dose and slower titration rate by reaching 6 mg/kg/24 hr by the end of 8 weeks. **$\geq 17$  yr and adult:** Use above initial dose and slower titration rate by reaching 200 mg BID by the end of 8 weeks; **max. dose:** 1600 mg/24 hr.**Monotherapy for partial-onset seizures or primary generalized tonic-clonic seizures:****Child 2– $<10$  yr:** Start with 25 mg PO QHS  $\times$  7 days. If needed and tolerated, may increase dose to 25 mg PO BID. May further increase by 25–50 mg/24 hr at weekly intervals over 5–7 weeks up to lower end of the following daily target maintenance dosing range. (If needed and tolerated, increase to higher end of dosing range by increasing by 25–50 mg/24 hr at weekly intervals.): **$\leq 11$  kg:** 150–250 mg/24 hr  $\div$  BID**12–22 kg:** 200–300 mg/24 hr  $\div$  BID**23–31 kg:** 200–350 mg/24 hr  $\div$  BID**32–38 kg:** 250–350 mg/24 hr  $\div$  BID **$>38$  kg:** 250–400 mg/24 hr  $\div$  BID**Child  $\geq 10$  yr and adult:** Start with 25 mg PO BID  $\times$  7 days, then increase by 50 mg/24-hr increments at 1-wk intervals up to a **max. dose** of 100 mg PO BID at wk 4. If needed, dose may be further increased at weekly intervals by 100 mg/24 hr up to a recommended **max. dose** of 200 mg PO BID.

Continued

TOPIRAMATE *continued*

**Use with caution** in renal and hepatic dysfunction (decreased clearance) and sulfa hypersensitivity. **Reduce dose by 50% when creatinine clearance is <70 mL/min.** Common side effects (incidence lower in children) include ataxia, cognitive dysfunction, dizziness, nystagmus, paresthesia, sedation, visual disturbances, nausea, dyspepsia, and kidney stones. Secondary angle-closure glaucoma characterized by ocular pain, acute myopia, and increased intraocular pressure has been reported and may lead to blindness if left untreated. Patients should be instructed to seek immediate medical attention if they experience blurred vision or periorbital pain. Oligohidrosis and hyperthermia have been reported, primarily in children, and should be monitored, especially during hot weather and with use of drugs that predispose patients to heat-related disorders (e.g., carbonic anhydrase inhibitors, anticholinergics). Hyperchloremic non-anion gap metabolic acidosis has also been reported. Suicidal behavior or ideation have been reported.

Drug is metabolized by and inhibits the CYP 450 2C19 isoenzyme. Phenytoin, valproic acid, and carbamazepine may decrease topiramate levels. Topiramate may decrease valproic acid, digoxin, and ethinyl estradiol (to decrease oral contraceptive efficacy) levels but may increase phenytoin levels. Alcohol and CNS depressants may increase CNS side effects. Carbonic anhydrase inhibitors (e.g., acetazolamide) may increase risk of metabolic acidosis, nephrolithiasis, or paresthesia. Use with valproic acid may result in development of hyperammonemia.

Safety and efficacy in migraine prophylaxis in pediatrics have not been established; an increase in serum creatinine has been reported in a clinical trial.

Doses may be administered with or without food. Capsule may be opened and sprinkled on small amount of food (e.g., 1 teaspoonful of applesauce) and swallowed whole (**do not chew**). Maintain adequate hydration to prevent kidney stone formation.

**TRAZODONE**

Many generics, previously available as Desyrel  
**Antidepressant, triazopyridine derivative**



Yes



Yes



2



C

**Tabs:** 50, 100, 150, 300 mg

**Depression (titrate to lowest effective dose [see remarks]):**

**Child (6–18 yr):** Start at 1.5–2 mg/kg/24 hr PO ÷ BID–TID. If needed, gradually increase dose Q3–4 days up to a **max. dose** of 6 mg/kg/24 hr ÷ TID.

**Alternative dosing for adolescent:** Start at 25–50 mg/24 hr. If needed, increase to 100–150 mg/24 hr in divided doses.

**Adult:** Start at 150 mg/24 hr PO ÷ TID. If needed, increase by 50 mg/24 hr Q3–4 days up to a **max. dose** of 600 mg/24 hr for hospitalized patients (400 mg/24 hr for ambulatory patients).

**Insomnia with comorbid psychiatric disorders (limited data):**

**18 mo–<3 yr:** Start at 25 mg PO QHS. If needed, increase by 25 mg Q2 week up to a **max.** of 100 mg/24 hr.

**3–5 yr:** Start at 50 mg PO QHS. If needed, increase by 25 mg Q2 week up to a **max.** of 150 mg/24 hr.

**5 yr–adolescent:** 25–50 mg PO QHS. If needed, increase by 25–50 mg Q2 week up to a **max.** of 200 mg/24 hr. Daily dose may be divided BID–TID when used for palliative care.



**Use with caution** in preexisting cardiac disease, initial recovery phase of MI, in patients receiving antihypertensive medications, renal and hepatic impairment (has not been evaluated), and electroconvulsive therapy. Common side effects include dizziness, drowsiness, dry mouth, and diarrhea. Seizures, tardive dyskinesia, EPS, arrhythmias, priapism, blurred vision, neuromuscular weakness, anemia, orthostatic hypotension, and



TRAZODONE *continued*

rash have been reported. Monitor for clinical worsening of depression and suicidal ideation/behavior after initiation of therapy or after dose changes.

Trazodone is a CYP 450 3A4 isoenzyme substrate (may interact with inhibitors and inducers) and may increase digoxin levels and increase CNS effects of alcohol, barbiturates, and other CNS depressants. **Max. antidepressant effect is seen at 2–6 wk.**

**TRETINOIN—TOPICAL PREPARATIONS**

Retin-A, Retin-A Micro, Avita, Renova, and many others

**Retinoic acid derivative, topical acne product**



No



No



2



C

**Cream:** 0.02% (40, 60 g), 0.025% (20, 45 g), 0.05% (20, 40 g), 0.0375% (35 g), 0.07% (35 g); may contain parabens

**Topical gel:** 0.01% (15, 45 g), 0.025% (15, 20, 45 g), 0.04% (20, 45, 50 g), 0.05% (45 g), 0.1% (20, 45, 50 g); may contain 90% alcohol, benzyl alcohol, and propylene glycol

**Topical:**

**Child > 12 yr and adult:** Gently wash face with a mild soap, pat skin dry, and wait 20–30 min before use. Initiate therapy with either 0.02% or 0.025% cream or 0.01% gel, and apply a small pea-sized amount to affected areas of face QHS or on alternate days. See remarks.

**Contraindicated** in sunburns. **Avoid** excessive sun exposure. If stinging or irritation occurs, decrease frequency of administration to every other day. **Avoid** contact with eyes, ears, nostrils, mouth, or open wounds. Local adverse effects include irritation, erythema, excessive dryness, blistering, crusting, hyperpigmentation or hypopigmentation, and acne flare-ups. Concomitant use of other topical acne products may lead to significant skin irritation. Onset of therapeutic benefits may be experienced within 2–3 wk, with optimal effects in 6 wk. Gel dosage form is flammable and should not be exposed to heat or temperatures >120°F.

**TRIAMCINOLONE**

Aristospan, Kenalog, Nasacort AQ, Oralone, Trianex, Triderm, and generics

**Corticosteroid**



Yes



Yes



2



C/D

**Nasal spray:**

**Nasacort AQ and generics:** 55 mcg/actuation (120 actuations per 16.5 g); contains benzalkonium chloride and EDTA

**Cream:**

**Triderm and generics:** 0.1% (15, 28.4, 30, 85.2, 454 g)

**Generics:** 0.025% (15, 80, 454 g), 0.5% (15 g)

**Ointment:**

**Trianex:** 0.05% (17, 85 g)

**Generics:** 0.025%, 0.1% (15, 80, 454 g), 0.5% (15 g)

**Lotion:** 0.025%, 0.1% (60 mL)

**Topical aerosol (Kenalog):** 0.2 mg/2-second spray (63, 100 g); contains 10.3% alcohol

**Dental paste (Oralone and generics):** 0.1% (5 g)

See Chapter 30 for potency rankings and sizes of topical preparations.

**Injection as acetanide:** 10 mg/mL (Kenalog-10) (5 mL), 40 mg/mL (Kenalog-40) (1, 5, 10 mL); contains benzyl alcohol

**Injection as hexacetanide:** 5 mg/mL (Aristospan Intralesional) (5 mL), 20 mg/mL (Aristospan Intraarticular) (1, 5 mL); contains benzyl alcohol

*Continued*

TRIAMCINOLONE *continued*

**Intranasal (titrate to lowest effective dose after symptoms are controlled; discontinue use if no relief of symptoms after 3 wk of use):**

**Nasacort AQ:**

**Child 2–5 yr:** 1 spray in each nostril once daily (110 mcg/24 hr; starting and **max. dose**).

**Child 6–11 yr:** Start with 1 spray in each nostril once daily (110 mcg/24 hr). If no benefit in 1 wk, dose may be increased to 2 sprays in each nostril once daily (220 mcg/24 hr). Decrease dose back to 1 spray in each nostril when symptoms are controlled.

**≥12 yr and adult:** 2 sprays in each nostril once daily (220 mcg/24 hr; starting and **max. dose**).

Decrease dose to 1 spray in each nostril when symptoms are controlled.

**Topical cream/ointment/lotion:**

**Child and adult:** Apply a thin film to affected areas BID–TID for topical concentrations of 0.1% or 0.5%, and BID–QID for 0.025% or 0.05%.

**Topical spray:**

**Child and adult:** Spray to affected area TID–QID.

**Intralesional:**

**≥12 yr and adult:**

**Acetonide salt (Kenalog-10; 10 mg/mL):** Up to 1 mg/site at intervals of 1 wk or more. May give separate doses in sites >1 cm apart, **not to exceed** 30 mg.

**Hexacetonide salt (Aristospan Intralesional; 5 mg/mL):** Up to 0.5 mg/square inch of affected skin (initial dose range: 2–48 mg). Additional injections should be administered according to patient response.

Rare reports of bone mineral density loss and osteoporosis have been reported with prolonged use of inhaled dosage form. Nasal preparations may cause epistaxis, cough, fever, nausea, throat irritation, dyspepsia, and fungal infections (rarely). Topical preparations may cause dermal atrophy, telangiectasias, and hypopigmentation. Anaphylaxis has been reported with use of injectable dosage form. Topical steroids should be **used with caution** on the face and in intertriginous areas. See Chapter 8.



Dosage adjustment for hepatic failure with systemic use may be necessary. **Use with caution** in thyroid dysfunction, respiratory TB, ocular herpes simplex, peptic ulcer disease, osteoporosis, hypertension, CHF, myasthenia gravis, ulcerative colitis, and renal dysfunction. With systemic use, pregnancy category changes to "D" if used during first trimester. Pregnancy category is "D" with ophthalmic route.

Shake intranasal dosage forms before each use. **Avoid** SC and IV administration with injectable dosage forms. Injectable forms contain benzyl alcohol. Avoid spraying eyes or inhaling topical aerosol dosage form.

**TRIAMTERENE**

Dyrenium

**Diuretic, potassium sparing**



Yes



Yes



?



C/D

**Caps:** 50, 100 mg; may contain benzyl alcohol and povidone

**Child:** 1–2 mg/kg/24 hr ÷ BID PO. May increase up to a **max. dose** of 3–4 mg/kg/24 hr up to 300 mg/24 hr.



**Adult:** 50–100 mg/24 hr ÷ once daily–BID PO; **max. dose:** 300 mg/24 hr.

**Do not use** if GFR < 10 mL/hr. **Adjust dose in renal impairment (see Chapter 31)** and cirrhosis. Monitor serum electrolytes. May cause hyperkalemia, hyponatremia, hypomagnesemia, and metabolic acidosis. Interstitial nephritis, thrombocytopenia, and anaphylaxis have been reported.



TRIAMTERENE *continued*

Concurrent use of ACE inhibitors may increase serum potassium. **Use with caution** when administering medications with high potassium load (e.g., some penicillins) and in patients with hepatic impairment or on high potassium diets. Cimetidine may increase effects. This drug is also available as a combination product with hydrochlorothiazide; erythema multiforme and toxic epidermal necrolysis have been reported with this combination product. Administer doses with food to minimize GI upset. Pregnancy category changes to "D" if used in pregnancy-induced hypertension.

## TRILISATE

See Choline Magnesium Trisalicylate

## TRIMETHOBENZAMIDE HCL

Tigan and generics

**Antiemetic**



Yes

Yes

?

?

**Caps:** 300 mg

**Injection:** 100 mg/mL (2, 20 mL); may contain phenol or parabens

**Child (PO):** 15–20 mg/kg/24 hr ÷ TID–QID

**Alternative dosing:**

<13.6 kg: 100 mg TID–QID

13.6–40 kg: 100–200 mg/dose TID–QID

>40 kg: 300 mg/dose TID–QID

**Adult:**

**PO:** 300 mg/dose TID–QID

**IM:** 200 mg/dose TID–QID



**Do not use** in premature or newborn infants. **Avoid** use in patients with hepatotoxicity, acute vomiting, or allergic reaction. CNS disturbances are common in children (extrapyramidal symptoms, drowsiness, confusion, dizziness). Hypotension, especially with IM use, may occur.



**IM not recommended in children.** Consider reducing dosage in the presence of renal impairment; significant amount of drug is excreted and eliminated by kidney.

FDA pregnancy category has not been formally assigned.

## TRIMETHOPRIM AND SULFAMETHOXAZOLE

See Sulfamethoxazole and Trimethoprim

## URSODIOL

Actigall, Urso 250, Urso Forte, and generics

**Gallstone solubilizing agent, cholelitholytic agent**




Yes

No

1

B

**Oral suspension:** 20, 25, 50, 60 mg/mL 

**Caps (Actigall and generics):** 300 mg

**Tabs:**

**Urso 250 and generics:** 250 mg

**Urso Forte and generics:** 500 mg

*Continued*



URSODIOL *continued***Biliary atresia:**

**Infant (limited data):** 10–15 mg/kg/24 hr once daily PO

**TPN-induced cholestasis:**

**Infant and child (limited data from Gastroenterology. 1996;111:716-719):** 30 mg/kg/24 hr ÷ TID PO

**Gallstone dissolution:**

**Adult:** 8–10 mg/kg/24 hr ÷ BID–TID PO

**Cystic fibrosis (to improve fatty acid metabolism in liver disease):**

**Child:** 15–30 mg/kg/24 hr ÷ BID–TID PO

**Contraindicated** in calcified cholesterol stones, radiopaque stones, bile pigment stones, or stones > 20 mm in diameter. **Use with caution** in patients with nonvisualizing gallbladder and chronic liver disease. May cause GI disturbance, rash, arthralgias, anxiety, headache, and elevated liver enzymes (elevated ALT, AST, alkaline phosphatase, bilirubin, GGT). Monitor LFTs Q mo for first 3 mo after initiating therapy and Q6 mo thereafter. Thrombocytopenia has been reported in clinical trials.

Aluminum-containing antacids, cholestyramine, and oral contraceptives decrease ursodiol effectiveness. Dissolution of stones may take several mo. Stone recurrence occurs in 30%–50% of patients within 5 yr.

**VALACYCLOVIR**

Valtrex and generics

**Antiviral agent**



Yes



Yes




1



B

**Tabs/Caplets:** 500, 1000 mg

**Oral suspension:** 50 mg/mL 

**Child:** Recommended dosages based on steady-state pharmacokinetic data in immunocompromised children. Efficacy data are incomplete.

**To mimic an IV acyclovir regimen of 250 mg/m<sup>2</sup>/dose or 10 mg/kg/dose TID:**

30 mg/kg/dose PO TID OR alternatively by weight:

**4–12 kg:** 250 mg PO TID

**13–21 kg:** 500 mg PO TID

**22–29 kg:** 750 mg PO TID

**≥30 kg:** 1000 mg PO TID

**To mimic a PO acyclovir regimen of 20 mg/kg/dose 4 or 5 times a day:**

20 mg/kg/dose PO TID OR alternatively by weight:

**6–19 kg:** 250 mg PO TID

**20–31 kg:** 500 mg PO TID

**≥32 kg:** 750 mg PO TID

**Chickenpox (immunocompetent patient; initiate therapy at earliest signs or symptoms within 24 hr of rash onset):**

**2–<18 yr:** 20 mg/kg/dose PO TID × 5 days; **max. dose:** 1 g/dose TID

**HSV treatment (immunocompetent):**

**3 mo–11 yr:** 20 mg/kg/dose PO BID; **max. dose:** 1000 mg/dose

**Herpes zoster (see remarks):**

**Adult (immunocompetent):** 1 g/dose PO TID × 7 days within 48–72 hours of onset of rash

**Genital herpes:**

**Adolescent and adult:**

**Initial episodes:** 1 g/dose PO BID × 10 days

*Continued*

VALACYCLOVIR *continued*

**Recurrent episodes:** 500 mg/dose PO BID  $\times$  3 days

**Suppressive therapy:**

**Immunocompetent patient:** 500–1000 mg/dose PO once daily  $\times$  1 year, then reassess for recurrences. Patients with  $<9$  recurrences/yr may be dosed at 500 mg/dose PO once daily  $\times$  1 yr.

**Herpes labialis (cold sores; initiated at earliest symptoms):**

$\geq 12$  yr and adult: 2 g/dose PO Q12 hr  $\times$  1 day

This prodrug is metabolized to acyclovir and L-valine, with better oral absorption than acyclovir.

**Use with caution in hepatic or renal insufficiency (adjust dose; see Chapter 31).**

Thrombotic thrombocytopenic purpura/hemolytic uremic syndrome (TTP/HUS) has been reported in patients with advanced HIV infection and in bone marrow and renal transplant recipients. Probenecid or cimetidine can reduce the rate of conversion to acyclovir. Headache, nausea, and abdominal pain are common adverse events in adults. Headache is common in children. See *Acyclovir* for additional drug interactions and adverse effects.

For initial episodes of genital herpes, therapy is most effective when initiated within 48 hr of symptom onset. Therapy should be initiated immediately after onset of symptoms in recurrent episodes (no efficacy data when initiating therapy  $>24$  hr after onset of symptoms). Data unavailable for use as suppressive therapy for periods  $>1$  yr.

Valacyclovir **CANNOT** be substituted for acyclovir on a one-to-one basis. Doses may be administered with or without food.

**VALGANCICLOVIR**

Valcyte

**Antiviral agent**



Yes



Yes



3



C

**Tabs:** 450 mg

**Oral solution:** 50 mg/mL (88 mL); contains saccharin and sodium benzoate

**Oral suspension:** 60 mg/mL

**Neonate and infant:**

**Symptomatic congenital CMV (from pharmacokinetic [PK] data in 8 infants 4–90 days old (mean, 20 days) and 24 neonates 8–34 days old):** 15–16 mg/kg/dose PO BID produced

similar levels to IV ganciclovir 6 mg/kg/dose BID. Additional PK, safety, and efficacy studies are required.

**Child (4 mo–16 yr):**

**CMV prophylaxis in kidney or heart transplantation (once-daily PO dosage is calculated with the following equation):**

Daily mg dose (**max. dose:** 900 mg) =  $7 \times \text{BSA} \times \text{CrCl}$ . BSA is determined by the Mosteller equation, and CrCl is determined by a modified Schwartz equation (**max. value:** 150 mL/min/1.73m<sup>2</sup>).

**Mosteller BSA (m<sup>2</sup>) equation:** Square root of [(height (cm)  $\times$  weight (kg))  $\div$  3600]

**Modified Schwartz (mL/min/1.73m<sup>2</sup>) equation (max. value: 150 mL/min/1.73m<sup>2</sup>):**  $k \times \text{height (cm)} \div \text{serum creatinine (mg/dL)}$ , where  $k = 0.45$  if patient is 4 mo to  $<2$  yr old;  $k = 0.55$  for boys  $2\text{--}13$  yr old and girls aged  $2\text{--}16$  yr old; or  $k = 0.7$  if boys  $13\text{--}16$  yr old.

**CMV prophylaxis in liver transplantation (limited data based on a retrospective review in 10 patients, mean age  $4.9 \pm 5.6$  yr):** 15–18 mg/kg/dose PO once daily  $\times$  100 days after transplantation resulted in 1 case of asymptomatic CMV infection detected by CMV antigenemia at day 7 of therapy. This patient then received a higher dose of 15 mg/kg/dose BID until 3 consecutive negative CMV antigenemia tests were achieved. Dose was switched back to a prophylactic regimen at day 46 post transplant.

*Continued*

VALGANCICLOVIR *continued***Adolescent (>16 yr) and adult:****CMV retinitis:****Induction therapy:** 900 mg PO BID  $\times$  21 days with food**Maintenance therapy:** 900 mg PO once daily with food**CMV prophylaxis in heart, kidney, and kidney-pancreas transplantation:** 900 mg PO once daily, starting within 10 days of transplantation until 100 days post heart or kidney-pancreas transplantation, or until 200 days post kidney transplantation.

This prodrug is metabolized to ganciclovir, with better oral absorption than ganciclovir.

**Contraindicated** with hypersensitivity to valganciclovir/ganciclovir, ANC < 500 mm<sup>3</sup>, platelets < 25,000 mm<sup>3</sup>, hemoglobin < 8 g/dL, and patients on hemodialysis. **Use with caution in renal insufficiency (adjust dose; see Chapter 31)**, preexisting bone marrow suppression, or receiving myelosuppressive drugs or irradiation. Has not been evaluated in hepatic impairment. May cause headache, insomnia, peripheral neuropathy, diarrhea, vomiting, neutropenia, anemia, and thrombocytopenia. Use effective contraception during and for at least 90 days after therapy; may impair fertility in men and women. See *Ganciclovir* for drug interactions and additional adverse effects.Valganciclovir **CANNOT** be substituted for ganciclovir on a one-to-one basis. All doses are administered with food. **Avoid** direct skin or mucous membrane contact with broken or crushed tablets.**VALPROIC ACID**

Depakene, Depacon, Stavzor, and various generics

[Depakote: See Divalproex Sodium]

**Anticonvulsant**

Yes



No



2



D/X

**Caps:** 250 mg**Delayed-release caps (Stavzor):** 125, 250, 500 mg**Syrup:** 250 mg/5 mL (473 mL); may contain parabens**Injection (Depacon):** 100 mg/mL (5mL)**Oral:****Initial:** 10–15 mg/kg/24 hr  $\div$  once daily–TID**Increment:** 5–10 mg/kg/24 hr at weekly intervals to **max. dose** of 60 mg/kg/24 hr**Maintenance:** 30–60 mg/kg/24 hr  $\div$  BID–TID. Owing to drug interactions, higher doses may be required in children on other anticonvulsants. If using divalproex sodium, administer BID.**IV (use only when PO is not possible):**Use same PO daily dose  $\div$  Q6 hr. Convert back to PO as soon as possible.**Rectal (use syrup diluted 1:1 with water, given PR as a retention enema):****Loading dose:** 20 mg/kg/dose**Maintenance:** 10–15 mg/kg/dose Q8 hr**Migraine prophylaxis:****Child (limited data):** 15–30 mg/kg/24 hr PO  $\div$  BID; alternative dosing for children  $\geq$ 12 yr is 250 mg PO BID (**max. dose:** 1000 mg/24 hr).**Adult:** Start with 500 mg/24 hr  $\div$  PO BID. Dose may be increased to a **max.** of 1000 mg/24 hr  $\div$  PO BID. If using divalproex sodium extended-release tablets, administer daily dose once daily.**Contraindicated** in hepatic disease, pregnancy (for migraine indication), mitochondrial disorders with mutations in DNA polymerase gamma (e.g., Alpers-Huttenlocher syndrome), and children <2 yr suspected of the aforementioned mitochondrial disorder. May cause GI, liver, blood, and CNS toxicity. May also cause weight gain, transient alopecia, pancreatitis*Continued*

VALPROIC ACID *continued*

(potentially life threatening), nausea, sedation, vomiting, headache, thrombocytopenia, platelet dysfunction, rash (especially with lamotrigine), and hyperammonemia. Hepatic failure has occurred, especially in children <2 yr (especially those receiving multiple anticonvulsants or with congenital metabolic disorders, severe seizure disorders with mental retardation, and organic brain disease). Idiosyncratic life-threatening pancreatitis has been reported in children and adults. Hyperammonemic encephalopathy has been reported in patients with urea cycle disorders. Suicidal behavior or ideation have been reported.

Valproic acid is a substrate for CYP 450 2C19 isoenzyme and an inhibitor of CYP 450 2C9, 2D6, and 3A3/4 (weak). It increases amitriptyline/nortriptyline, phenytoin, diazepam, and phenobarbital levels. Concomitant phenytoin, phenobarbital, topiramate, meropenem, and carbamazepine may decrease valproic acid levels. Amitriptyline or nortriptyline may increase valproic acid levels. May interfere with urine ketone and thyroid tests.

**Do not give** syrup with carbonated beverages. Use of IV route has not been evaluated for > 14 days of continuous use. Infuse IV over 1 hr up to a **max. rate** of 20 mg/min. Depakote and Depakote ER are **NOT** bioequivalent; see package insert for dose conversion.

**Therapeutic levels:** 50–100 mg/L. Recommendations for serum sampling at steady state: Obtain trough level within 30 min before next scheduled dose after 2–3 days of continuous dosing. Levels of 50–60 mg/L and as high as 85 mg/L have been recommended for bipolar disorders. Monitor CBC and LFTs before and during therapy.

Valproic acid and divalproex should not be used in pregnant women. Increased risk of neural tube defects, decreased child IQ scores, craniofacial defects, and cardiovascular malformations have been reported in babies exposed to valproic acid and divalproex sodium.

Pregnancy category is "X" when used for migraine prophylaxis and "D" for all other indications.

**VALSARTAN**

Diovan

**Angiotensin II receptor blocker, antihypertensive agent**

Yes



Yes



?



D

**Tabs:** 40, 80, 160, 320 mg**Oral suspension:** 4 mg/mL **Hypertension (see remarks):**

**Child 1–5 yr (≥8 kg, limited data):** a reported range of 0.4–3.4 mg/kg/dose PO once daily, with the following maximum doses:

<18 kg: 40 mg/24 hr

≥18 kg: 80 mg/24 hr

**Child 6–16 yr:** Start at 1.3 mg/kg/dose (**max. dose:** 40 mg) PO once daily. Dose may be increased up to 2.7 mg/kg/dose up to 160 mg; doses greater than this have not been studied.

**Adolescent ≥ 17 yr and adult (non–volume-depleted status):** Start at 80 or 160 mg PO once daily; usual dose range is 80–320 mg once daily. **Max. dose:** 320 mg/24 hr.

**Contraindicated** with aliskiren use in diabetic patients. Discontinue use immediately after pregnancy is detected. **Use with caution** in renal and liver insufficiency (no data available), heart failure, post MI, renal artery stenosis, renal function changes, and volume depletion.

Hypotension, dizziness, headache, cough, and increases in BUN and SCr are common side effects.

Hyperkalemia, angioedema, acute renal failure, and dysgeusia have been reported.

Onset of initial antihypertensive effects is 2 hr, with max. effects after 2–4 wk of chronic use. Patients may require higher doses of oral tablet dosage form than oral suspension (increased bioavailability with oral suspension).



**VANCOMYCIN**

Vancocin and generics

**Antibiotic, glycopeptide**

No



Yes



2



C/B

**Injection:** 0.5, 0.75, 1, 5, 10 g**Premixed injection:** 500 mg/100 mL in dextrose, 750 mg/150 mL in dextrose, 1000 mg/200 mL in dextrose (iso-osmotic solutions)**Caps:** 125, 250 mg**Oral solution:** 25 mg/mL 

Initial empirical dosage; patient-specific dosage defined by therapeutic drug monitoring (see remarks).

**Neonate, IV (see following table for dosage interval):****Bacteremia:** 10 mg/kg/dose**Meningitis, pneumonia:** 15 mg/kg/dose

Postmenstrual Age (wk)*	Postnatal Age (days)	Dosage Interval (hr)
≤29	0–14	18
	>14	12
30–36	0–14	12
	>14	8
37–44	0–7	12
	>7	8
≥45	All	6

\*Postmenstrual age = gestational age + postnatal age.

**Infant, child, adolescent, and adult, IV:**

Age	General Dosage	CNS Infections, Endocarditis, Osteomyelitis, Pneumonia, and MRSA Bacteremia
1 mo–12 yr	15 mg/kg Q6 hr	20 mg/kg Q6 hr
Adolescent	15 mg/kg Q6–8 hr	20 mg/kg Q6–8 hr
Adult	15 mg/kg Q8–12 hr	20 mg/kg Q8–12 hr

**Clostridium difficile colitis:****Child:** 40–50 mg/kg/24 hr ÷ Q6 hr PO × 7–10 days**Max. dose:** 500 mg/24 hr; higher max. of 2 g/24 hr has also been used.**Adult:** 125 mg/dose PO Q6 hr × 7–10 days; dosages as high as 2 g/24 hr ÷ Q6–8 hr have also been used.**Endocarditis prophylaxis for GU or GI (excluding esophageal) procedures (complete all antibiotic dose infusion[s] within 30 min of starting procedure):****Moderate-risk patients allergic to ampicillin or amoxicillin:****Child:** 20 mg/kg/dose IV over 1–2 hr × 1**Adult:** 1 g/dose IV over 1–2 hr × 1**High-risk patients allergic to ampicillin or amoxicillin:****Child and adult:** Same dose as moderate-risk patients plus gentamicin 1.5 mg/kg/dose (max. dose: 120 mg/dose) IV/IM × 1

Ototoxicity and nephrotoxicity may occur and may be exacerbated with concurrent aminoglycoside use. Greater nephrotoxicity risk has been associated with higher therapeutic serum trough concentrations ( $\geq 15$  mg/mL) and receiving furosemide in the ICU. **Adjust dose in renal failure (see Chapter 31).** Use total body weight for obese patients when calculating dosages. Low concentrations of the drug may appear in CSF with inflamed meninges. Nausea,



Continued

VANCOMYCIN *continued*

vomiting, and drug-induced erythroderma are common with IV use. "Red man syndrome" associated with rapid IV infusion may occur. Infuse over 60 min (may infuse over 120 min if 60-min infusion is not tolerated). **Note:** Diphenhydramine is used to reverse red man syndrome. Allergic reactions (including drug rash with eosinophilia and systemic symptoms [DRESS]), neutropenia, and immune-mediated thrombocytopenia have been reported.

Although current extrapolated adult guidelines suggest measuring only trough levels, an additional post-distributional level may be useful in characterizing enhanced/altered drug clearance for quicker dosage modification to attain target levels. This may be useful for infants with known faster clearance and patients in renal compromise. Consult a pharmacist.

The following therapeutic trough level recommendations are based on the assumption that the pathogen's vancomycin MIC is  $\leq 1$  mg/L.

Indication	Goal Trough Level
Uncomplicated skin and soft tissue infection, non-MRSA bacteremia, febrile neutropenia	10–15 mg/L
CNS infections, endocarditis, pneumonia, osteomyelitis, MRSA bacteremia	15–20 mg/L

Peak level measurement (20–50 mg/L) has also been recommended for patients with burns, clinically nonresponsive in 72 hr of therapy, persistent positive cultures, and CNS infections ( $\geq 30$  mg/L).

**Recommended serum sampling time at steady state:** Trough within 30 min before fourth consecutive dose and peak 60 min after administration of fourth consecutive dose. Infants with faster elimination (shorter  $T_{1/2}$ ) may be sampled around third consecutive dose.

**ORAL USE:** Metronidazole (PO) is the drug of choice for *C. difficile* colitis; vancomycin should be avoided owing to emergence of vancomycin-resistant enterococcus. Common adverse effects with oral vancomycin capsules in adults include nausea, abdominal pain, and hypokalemia.

Pregnancy category "B" is assigned with the oral route of administration.

**VARICELLA-ZOSTER IMMUNE GLOBULIN (HUMAN)**

VariZig, VZIG

*Hyperimmune globulin, varicella-zoster*



No



No



2



C

**Injection:** 125 U; contains 60–200 mg human immunoglobulin (Ig)G, 0.1 M glycine, 0.04 M sodium chloride, and 0.01% polysorbate 80. A vial of 8.5 mL sterile diluent is provided.

**Dose should be given within 48 hr of varicella exposure and no later than 96 hr post exposure. IM (preferred route) or IV (see remarks):**

<2 kg: 62.5 U

2.1–10 kg: 125 U

10.1–20 kg: 250 U

20.1–30 kg: 375 U

30.1–40 kg: 500 U

>40 kg: 625 U

**Max. dose:** 625 U/dose

If patient is high risk and reexposed to varicella for >3 weeks after a prior dose, another full dose may be given.

**Contraindicated** in severe thrombocytopenia (risk with IM injection), IgA deficiency (anaphylactic reactions may occur), and known immunity to varicella-zoster virus. See Chapter 16 for indications. Local discomfort, redness, and swelling at injection site and headache may occur.



*Continued*

VARICELLA-ZOSTER IMMUNE GLOBULIN (HUMAN) *continued*

Hyperviscosity of blood may increase risk for thrombotic events. IM route is preferred over IV in patients with preexisting respiratory conditions. Interferes with immune response to live virus vaccines such as measles, mumps, and rubella; defer administration of live vaccines 6 mo or longer after VZIG dose. See latest AAP *Red Book* for additional information.

IM route is the preferred route by diluting each vial with 1.25 mL of diluent for a 100 U/mL concentration. **Avoid** IM injection into the gluteal region (risk for sciatic nerve damage), and **do not exceed** age-specific **single max. IM injection** volume. For IV administration, dilute each vial with 2.5 mL of diluent for a 50 U/mL concentration. IV doses are administered over 3–5 min.

**VASOPRESSIN**

Pitressin and various generics, 8-Arginine Vasopressin

**Antidiuretic hormone analog**



Yes



No



2



C

**Injection:** 20 U/mL (aqueous) (0.5, 1, 10 mL); may contain 0.5% chlorbutanol

**Diabetes insipidus:** Titrate dose to effect.

**SC/IM:**

**Child:** 2.5–10 U BID–QID

**Adult:** 5–10 U BID–QID

**Continuous infusion (adult and child):** Start at 0.5 mU/kg/hr (0.0005 U/kg/hr). Double dosage every 30 min PRN up to **max. dose** of 10 mU/kg/hr (0.01 U/kg/hr).

**Growth hormone and corticotropin provocative tests:**

**Child:** 0.3 U/kg IM; **max. dose:** 10 U

**Adult:** 10 U IM

**GI hemorrhage (IV; Note: dosage metric is U/kg/min for children and U/min for adults):**

**Child:** Start at 0.002–0.005 U/kg/min. Increase dose as needed to **max. dose** of 0.01 U/kg/min.

**Adult:** Start at 0.2–0.4 U/min. Increase dose as needed to **max. dose** of 0.8 U/min.

**Cardiac arrest, ventricular fibrillation, and pulseless ventricular tachycardia:**

**Child (use after 2 doses of epinephrine; limited data):** 0.4 U/kg IV  $\times$  1

**Adult:** 40 U IV or IO  $\times$  1

**Vasodilatory shock with hypotension (unresponsive to fluids and pressors. Note: dosage metric is U/kg/min for children and U/min for adults):**

**Infant, child, adolescent (various reports):** 0.00017–0.008 U/kg/min via continuous IV infusion in combination with pressors.

**Adult:** 0.01–0.04 U/min via continuous IV infusion in combination with pressors.

**Use with caution** in seizures, migraine, asthma, and renal, cardiac, or vascular diseases. Side effects include tremor, sweating, vertigo, abdominal discomfort, nausea, vomiting, urticaria, anaphylaxis, hypertension, and bradycardia. May cause vasoconstriction, water intoxication, and bronchoconstriction. Drug interactions: lithium, demeclocycline, heparin, and alcohol reduce activity; carbamazepine, tricyclic antidepressants, fludrocortisone, and chlorpropamide increase activity.

**Do not** abruptly discontinue IV infusion (taper dose). Patients with variceal hemorrhage and hepatic insufficiency may respond to lower dosages. Monitor fluid intake and output, urine specific gravity, urine and serum osmolality, and sodium.

**VECURONIUM BROMIDE**

Various generics; previously available as Norcuron  
**Nondepolarizing neuromuscular blocking agent**



Yes



Yes



?



C

**Injection:** 10, 20 mg; diluent for reconstitution may contain benzyl alcohol.

**Neonate:**

**Initial:** 0.1 mg/kg/dose IV

**Maintenance:** 0.03–0.15 mg/kg/dose IV Q1–2 hr PRN

**Infants (>7 wk–1 yr) (see remarks):**

**Initial:** 0.08–0.1 mg/kg/dose IV

**Maintenance:** 0.05–0.1 mg/kg/dose IV Q1 hr PRN; may administer via continuous infusion at 0.06–0.09 mg/kg/hr IV.

**>1 yr–adult (see remarks):**

**Initial:** 0.08–0.1 mg/kg/dose IV

**Maintenance:** 0.05–0.1 mg/kg/dose IV Q1 hr PRN; may administer via continuous infusion at 0.09–0.15 mg/kg/hr IV.

**Use with caution** in patients with neuromuscular disease and renal or hepatic impairment.

Dose reduction may be necessary in hepatic insufficiency. Infants (7 wk–1 yr) are more sensitive to the drug and may have a longer recovery time. Children (1–10 yr) may require higher doses and more frequent supplementation than adults. Enflurane, isoflurane, aminoglycosides,  $\beta$ -blockers, calcium channel blockers, clindamycin, furosemide, magnesium salts, quinidine, procainamide, and cyclosporine may increase potency and duration of neuromuscular blockade. Calcium, caffeine, carbamazepine, phenytoin, steroids (chronic use), acetylcholinesterases, and azathioprine may decrease effects. May cause arrhythmias, rash, and bronchospasm. Severe anaphylactic reactions have been reported.

**Neostigmine, pyridostigmine, or edrophonium are antidotes.** Onset of action within 1–3 min. Duration is 30–40 min. **See Chapter 1 for rapid sequence intubation.**

**VERAPAMIL**

Calan, Calan SR, Isoptin SR, Verelan, Verelan PM, and generics  
**Calcium channel blocker**



Yes



Yes



2



C

**Tabs:** 40, 80, 120 mg

**Extended/sustained-release tabs:** 120, 180, 240 mg

**Extended/sustained-release caps (for Q24 hr dosing):** 100, 120, 180, 200, 240, 300, 360 mg

**Injection:** 2.5 mg/mL (2, 4 mL)

**Oral suspension:** 50 mg/mL

**IV for dysrhythmias:** Give over 2–3 min. May repeat once after 30 min.

**1–16 yr, for PSVT:** 0.1–0.3 mg/kg/dose  $\times$  1; may repeat dose in 30 min; **max. dose:** 5 mg first dose, 10 mg second dose

**Adult, for SVT:** 5–10 mg (0.075–0.15 mg/kg)  $\times$  1; may administer second dose of 10 mg (0.15 mg/kg) 15–30 min later

**PO for hypertension:**

**Child:** 4–8 mg/kg/24 hr  $\div$  TID or by age:

**1–5 yr:** 40–80 mg Q8 hr

**>5 yr:** 80 mg Q6–8 hr

**Adult:** 240–480 mg/24 hr  $\div$  TID–QID, or divide once daily–BID for sustained-release preparations

*Continued*



VERAPAMIL *continued*

**Contraindications** include hypersensitivity, cardiogenic shock, severe CHF, sick sinus syndrome, or AV block. **Use with caution** in hepatic and renal impairment (**reduce dose in renal insufficiency [see Chapter 31]**). **Owing to negative inotropic effects, verapamil should not be used to treat SVT in an emergency setting in infants. Avoid IV use** in neonates and young infants; may cause apnea, bradycardia, and hypotension. May cause constipation, headache, dizziness, edema, and hypotension. EPS has been reported.

**Monitor ECG. Have calcium and isoproterenol available to reverse myocardial depression.** May decrease neuromuscular transmission in patients with Duchenne muscular dystrophy and worsen myasthenia gravis.

Drug is a substrate of CYP 450 1A2 and 3A4/5, and an inhibitor of CYP 3A4 and P-gp transporter. Barbiturates, sulfonpyrazole, phenytoin, vitamin D, and rifampin may decrease serum levels/effects of verapamil; quinidine and grapefruit juice may increase serum levels/effects. Verapamil may increase effects/toxicity of  $\beta$ -blockers (severe myocardial depression), carbamazepine, cyclosporine, digoxin, ethanol, fentanyl, lithium, nondepolarizing muscle relaxants, prazosin, and tizanidine. Use with telithromycin has resulted in hypotension, bradyarrhythmias, and lactic acidosis. Bradycardia has been reported with concurrent use of clonidine, and increased bleeding times have been reported when used with aspirin.

**VIGABATRIN**

Sabril

**Anticonvulsant**

Yes



Yes



?



C

**Tabs:** 500 mg**Powder for oral solution:** 500 mg per packet to be dissolved in 10 mL water (50s)

**Infantile spasms (1 mo–2 yr; see remarks for discontinuation of therapy):** Start at 50 mg/kg/24 hr  $\div$  BID PO. If needed and tolerated, may titrate dosage upwards by 25–50 mg/kg/24 hr increments Q3 days up to a **max.** of 150 mg/kg/24 hr  $\div$  BID.

**Adjunctive therapy for refractory complex partial seizures (see remarks for discontinuation of therapy):**

**Child ( $\geq 10$  kg):** Start at 40 mg/kg/24 hr  $\div$  BID PO. If needed and tolerated, adjust dose to the following maintenance dose:

**10–15 kg:** 500–1000 mg/24 hr  $\div$  BID

**16–30 kg:** 1000–1500 mg/24 hr  $\div$  BID

**31–50 kg:** 1500–3000 mg/24 hr  $\div$  BID

**>50 kg:** 2000–3000 mg/24 hr  $\div$  BID

**Adolescent ( $\geq 16$  yr) and adult (see remarks for discontinuation of therapy):** Start at 500 mg BID PO. If needed and tolerated, increase daily dose by 500-mg increments at 7-day intervals. Usual dose: 1500 mg BID. **Max. dose:** 6000 mg/24 hr. Doses  $>3$  g/24 hr have not been shown to provide additional benefit and are associated with more side effects.

**Use with caution** in renal impairment (**reduce dose [see Chapter 31]**) and with other CNS depressants (enhanced effects). Can cause progressive and permanent vision loss (risk increases with dose and duration); periodic vision testing is required. Common side effects include rash, weight gain, GI disturbances, arthralgia, visual disturbances, vertigo, sedation, headache, confusion, and URI. Liver failure, anemia, psychotic disorder, angioedema, Stevens-Johnson syndrome, and suicidal ideation have been reported. Dose-dependent abnormal MRIs have been reported in infants treated for infantile spasms.

Ketorolac, naproxen, and mefloquine may decrease effect of vigabatrin. Vigabatrin may decrease effects/levels of phenytoin but increase levels/toxicity of carbamazepine.

*Continued*

VIGABATRIN *continued*

**DO NOT** rapidly withdraw therapy. Dosage must be tapered when discontinuing therapy to minimize increased seizure frequency. The following tapering guidelines have been recommended:

**Infant and child:** Decrease by 25–50 mg/kg every 3–4 days.

**Adult:** Decrease by 1 g/24 hr every 7 days.

Doses may be administered with or without food. Access to this medication is restricted to prescribers and pharmacies registered under a special restricted distribution program (SHARE) in the United States. Call 888–45-SHARE for more information.

**VITAMIN A**

Aquasol A and many generics

**Vitamin, fat-soluble**



No



No



2



A/X

**Caps [OTC]:** 8,000, 10,000, 25,000 IU

**Tabs [OTC]:** 5,000, 10,000 IU

**Injection (Aquasol A):** 50,000 IU/mL (2 mL); contains polysorbate 80 and chlorobutanol

**U.S. RDA:** See Chapter 21.

**Supplementation in measles (see remarks):**

**<6 mo:** 50,000 IU/dose once daily PO  $\times$  2 days. Repeat 1 dose at 4 wk.

**6 mo–1 yr:** 100,000 IU/dose once daily PO  $\times$  2 days. Repeat 1 dose at 4 wk.

**1–2 yr:** 200,000 IU/dose once daily PO  $\times$  2 days. Repeat 1 dose at 4 wk.

**Malabsorption syndrome prophylaxis:**

**Child > 8 yr and adult:** 10,000–50,000 IU/dose once daily PO of water-miscible product

**High doses above the U.S. RDA are teratogenic (category X).** Use of vitamin A in measles is recommended in children 6 mo–2 yr of age who are either hospitalized or have any of the following risk factors: immunodeficiency, ophthalmologic evidence of vitamin A deficiency, impaired GI absorption, moderate to severe malnutrition, and recent immigration from areas with high measles mortality. May cause GI disturbance, rash, headache, increased ICP (pseudotumor cerebri), papilledema, and irritability. Large doses may increase effects of warfarin. Mineral oil, cholestyramine, and neomycin will reduce vitamin A absorption. Do not access vitamin A levels during an acute inflammatory condition as falsely low levels have been reported. **See Chapter 21 for multivitamin preparations.**

**VITAMIN B<sub>1</sub>**

See *Thiamine*

**VITAMIN B<sub>2</sub>**

See *Riboflavin*

**VITAMIN B<sub>3</sub>**

See *Niacin*

**VITAMIN B<sub>6</sub>**See *Pyridoxine***VITAMIN B<sub>12</sub>**See *Cyanocobalamin***VITAMIN C**See *Ascorbic Acid***VITAMIN D<sub>2</sub>**See *Ergocalciferol***VITAMIN D<sub>3</sub>**See *Cholecalciferol***VITAMIN E/α-TOCOPHEROL**

Aquasol E, Aquavit-E, Nutr-E-Sol, and others

*Vitamin, fat soluble*

No



No



2



A/C

**Tabs [OTC]:** 100, 200, 400 IU**Caps [OTC]:** 100, 200, 400, 600, 1000 IU**Oral solution (Aquasol E, Aquavit-E) [OTC]:** 50 IU/mL (12, 30 mL); may contain propylene glycol, polysorbate 80, and saccharin**Oral liquid (Nutr-E-Sol) [OTC]:** 400 IU/15 mL (473 mL)**U.S. RDA:** See Chapter 21.**Vitamin E deficiency, PO:** Follow levels.

Use water-miscible form with malabsorption.

**Neonate:** 25–50 IU/24 hr × 1 week, followed by recommended dietary intake**Child:** 1 IU/kg/24 hr**Adult:** 60–75 IU/24 hr**Cystic fibrosis (use water-miscible form):** 5–10 IU/kg/24 hr PO once daily. **Max. dose:** 400 IU/24 hr.

Adverse reactions include GI distress, rash, headache, gonadal dysfunction, decreased serum thyroxine and triiodothyronine, and blurred vision. Necrotizing enterocolitis has been associated with large doses (>200 units/24 hr) of a hyperosmolar product administered to low-birth-weight infants. May increase hypoprothrombinemic response of oral anticoagulants (e.g., warfarin), especially in doses >400 IU/24 hr.

One unit of vitamin E = 1 mg of dl-α-tocopherol acetate. In malabsorption, water-miscible preparations are better absorbed. Therapeutic levels: 6–14 mg/L.

Pregnancy category changes to "C" if used in doses above the RDA. **See Chapter 21 for multivitamin preparations.**



## VITAMIN K

See *Phytonadione*

## VORICONAZOLE

Vfend and generics

Antifungal, triazole



Yes



Yes



?



D

**Tabs:** 50, 200 mg; contains povidone**Oral suspension:** 40 mg/mL (75 mL); may contain sodium benzoate**Injection:** 200 mg; contains 3200 mg sulfobutyl ether  $\beta$ -cyclodextrin (SBECD)**Empirical doses. Between-patient and inter-occasion pharmacokinetic variability is high.****Monitor trough level, and adjust dose accordingly.** See [www.clinicaltrials.gov](http://www.clinicaltrials.gov) for updated dosing information.**<2 yr (limited data):** 9 mg/kg/dose IV/PO Q12 hr**2–11 yr (limited data [see remarks]):** 7–9 mg/kg/dose IV/PO Q12 hr. **Max. initial dose:** 350 mg/dose.**Invasive aspergillosis, invasive candidiasis, or other rare molds (e.g., *Scedosporium* and *Fusarium*)—including 12–14-yr-olds weighing <50 kg; dosing based on a previous clinical trial that was terminated because of slow enrollment:**9 mg/kg/dose IV Q12 hr  $\times$  2 doses, followed by 8 mg/kg/dose IV Q12 hr. Convert to oral therapy when significant clinical improvement after 1 week of IV therapy at a dose of 9 mg/kg/dose PO Q12 hr (**max. dose:** 350 mg Q12 hr).**Esophageal candidiasis—including 12–14-yr-olds weighing <50 kg; dosing based on a previous clinical trial that was terminated because of slow enrollment:****IV:** 4 mg/kg/dose Q12 hr**PO:** 9 mg/kg/dose Q12 hr; **max. dose:** 350 mg Q12 hr**Prophylaxis in pediatric acute leukemia (regimen currently being evaluated):** 6 mg/kg/dose PO Q12 hr  $\times$  2 doses, followed by 4 mg/kg/dose PO Q12 hr **$\geq$  12 yr and adolescent:****Invasive aspergillosis, invasive candidiasis, or other rare molds (e.g., *Scedosporium* and *Fusarium*)—excluding 12–14-yr-olds weighing <50 kg; dosing based on a previous clinical trial that was terminated because of slow enrollment:**6 mg/kg/dose IV Q12 hr  $\times$  2 doses, followed by 4 mg/kg/dose IV Q12 hr. Convert to oral therapy when significant clinical improvement after 1 week of IV therapy at a dose of 200 mg PO Q12 hr. For patients weighing <50 kg, use 2–11-yr dosing regimen. Alternatively, use adult PO dosage.**Esophageal candidiasis—excluding 12–14-yr-olds weighing <50 kg; use 2–11-yr dosing regimen for patients <50 kg; dosing based on a previous clinical trial that was terminated because of slow enrollment:****IV:** 3 mg/kg/dose Q12 hr**PO:** 200 mg Q12 hr; alternatively, use adult PO dosage.**Prophylaxis in pediatric acute leukemia (up to 15 yr old); regimen currently being evaluated:**6 mg/kg/dose PO Q12 hr  $\times$  2 doses, followed by 4 mg/kg/dose PO Q12 hr**Adult:****Invasive aspergillosis, candidemia, *Fusarium*/scedosporiosis, or other serious fungal infections:****Loading dose:** 6 mg/kg/dose IV Q12 hr  $\times$  2 doses**Maintenance dose:****Candidemia:** 3–4 mg/kg/dose IV Q12 hr**Invasive aspergillosis, *Fusarium*/scedosporiosis, or other serious fungal infections:** 4 mg/kg/dose IV Q12 hr. If patient unable to tolerate, reduce dose to 3 mg/kg/dose IV Q12 hr.

Continued

VORICONAZOLE *continued*

**PO maintenance dose:** Initial dose may be increased to max. dose when response is inadequate. If dose is not tolerated, reduce dose by 50-mg increments until tolerated, with minimum of initial recommended dose.

**<40 kg:** 100 mg Q12 hr; **max. dose:** 300 mg/24 hr

**≥40 kg:** 200 mg Q12 hr; **max. dose:** 600 mg/24 hr

**Esophageal candidiasis (treat for a minimum of 14 days and until 7 days after resolution of symptoms):** Initial dose may be increased to max. dose when response is inadequate. If dose is not tolerated, reduce dose by 50-mg increments until tolerated, with minimum of initial recommended dose.

**<40 kg:** 100 mg Q12 hr; **max. dose:** 300 mg/24 hr

**≥40 kg:** 200 mg Q12 hr; **max. dose:** 600 mg/24 hr

**Contraindicated** with concomitant administration of CYP 450 3A4 substrates that can lead to prolonged QTc interval (e.g., cisapride, pimozide, quinidine); concomitant administration of rifampin, carbamazepine, barbiturates, ritonavir, efavirenz, rifabutin, and St. John's wort (decreases voriconazole levels); and concomitant administration of sirolimus, efavirenz, rifabutin, and ergot alkaloids (voriconazole increases levels of these drugs). Drug is a substrate and inhibitor of CYP 450 2C9, 2C19 (major substrate), and 3A4 isoenzymes. **Use with caution** in severe hepatic disease and galactose intolerance.



Currently approved for use in invasive aspergillosis, candidal esophagitis, and *Fusarium* and *Scedosporium apiospermum* infections. Common side effects include GI disturbances, fever, headache, hepatic abnormalities, photosensitivity (avoid direct sunlight), rash (6%), and visual disturbances (30%). Serious but rare side effects include anaphylaxis, liver or renal failure, and Stevens-Johnsons syndrome. Pancreatitis has been reported in children.

**Adjust dose in hepatic impairment** by decreasing only the maintenance dose by 50% for patients with a Child-Pugh class A or B. **Do not use** IV dosage form for patients with GFR <50 mL/min because of accumulation of the cyclodextrin excipient; switch to oral therapy if possible. Patients receiving concurrent phenytoin should increase their voriconazole maintenance doses (IV: 5 mg/kg/dose Q12 hr; PO: double the usual dose).

See [www.clinicaltrials.gov](http://www.clinicaltrials.gov) for updated pediatric clinical trial information. Inter-occasion pharmacokinetic variability is high, requiring serum level monitoring. Therapeutic levels: trough, 1–5.5 mg/L. Levels <1 mg/L have resulted in treatment failures, and levels >5.5 mg/L have resulted in neurotoxicity (e.g., encephalopathy). Recommended serum sampling time: Obtain trough within 30 min before a dose. Steady state is typically achieved 5–7 days after initiating therapy. Administer IV over 1–2 hr, with a **max. rate** of 3 mg/kg/hr at a concentration ≤5 mg/mL. Administer oral doses 1 hr before and after meals.

**WARFARIN**

Coumadin, Jantoven, and generics

**Anticoagulant**



Yes



Yes



1



X

**Tabs:** 1, 2, 2.5, 3, 4, 5, 6, 7.5, 10 mg

**Injection:** 5 mg

**Infant and child (see remarks), to achieve an INR between 2 and 3:**

**Loading dose on day 1:**

**Baseline INR ≤ 1.3:** 0.2 mg/kg/dose PO; **max. dose:** 7.5 mg/dose

**Liver dysfunction, baseline INR > 1.3, undergone Fontan procedure, NPO status/poor nutrition, receiving broad-spectrum antibiotics, receiving medications that significantly inhibit CYP 450 2C9 or slow metabolizers of warfarin (see remarks):** 0.1 mg/kg/dose PO; **max. dose:** 5 mg/dose



*Continued*

WARFARIN *continued***Loading dose on days 2–4:**

If INR 1.1–1.3: Repeat day 1 loading dose.

If INR 1.4–1.9: Decrease day 1 loading dose by 50%.

If INR 2–3: Decrease day 1 loading dose by 50%.

If INR 3.1–3.5: Decrease day 1 loading dose by 75%.

If INR > 3.5: Hold doses until INR < 3.5, and restart at 50% of previous dose.

**Maintenance dose (therapy day ≥ 5):**

If INR 1.1–1.4: Increase previous dose by 20%.

If INR 1.5–1.9: Increase previous dose by 10%.

If INR 2–3: No change.

If INR 3.1–3.5: Decrease previous dose by 10%.

If INR > 3.5: Hold doses until INR < 3.5, and restart at 20% less than the last dose.

**Usual maintenance dose:** ≈0.1 mg/kg/24 hr PO once daily; range, 0.05–0.34 mg/kg/24 hr. (See remarks.)

**Adult (see remarks):** 5–10 mg PO once daily × 2–5 days. Adjust dose to achieve the desired INR or PT.

**Maintenance dose range:** 2–10 mg/24 hr PO once daily

**Contraindicated** in severe liver or kidney disease, uncontrolled bleeding, GI ulcers, and malignant hypertension. Acts on vitamin K–dependent coagulation factors II, VII, IX, and X. Side effects include fever, skin lesions, skin necrosis (especially in protein C deficiency), anorexia, nausea, vomiting, diarrhea, hemorrhage, and hemoptysis.



Warfarin is a substrate for CYP 450 1A2, 2C8, 2C9, 2C18, 2C19, and 3A3/4. Chloramphenicol, chloral hydrate, cimetidine, delavirdine, fluconazole, fluoxetine, metronidazole, indomethacin, large doses of vitamins A or E, NSAIDs, omeprazole, oxandrolone, quinidine, salicylates, SSRIs (e.g., fluoxetine, paroxetine, sertraline), sulfonamides, and zafirlukast may increase warfarin's effect. Ascorbic acid, barbiturates, carbamazepine, cholestyramine, dicloxacillin, griseofulvin, oral contraceptives, rifampin, spironolactone, sucralfate, and vitamin K (including foods with high content) may decrease warfarin's effect.

Younger children generally require higher doses to achieve desired effect. A cohort study of 319 children found that infants <1 yr required an average daily dose of 0.33 mg/kg, and teenagers 11–18 yr required 0.09 mg/kg to maintain a target INR of 2–3. Children receiving Fontan cardiac surgery may require smaller doses than children with either congenital heart disease (without Fontan) or no congenital heart disease. (See *Chest*. 2004;126:645–687S and *Blood*. 1999;94:3007–3014 for additional information.)

Lower initial doses should be considered for patients with pharmacogenetic variations in CYP 2C9 (e.g., \*2 and \*3 alleles) and VKORC1 (e.g., 1639G>A allele) enzymes, elderly and/or debilitated patients, and patients with a potential to exhibit greater than expected PT/INR response to warfarin.

The INR (international normalized ratio) is the recommended test to monitor warfarin anticoagulant effect. It takes 5–7 days for an INR to reach steady state on a consistent dosing schedule. The particular INR desired is based upon the indication and has been extrapolated from adults. An INR of 2–3 has been recommended for prophylaxis and treatment of DVT, pulmonary emboli, and bioprosthetic heart valves. An INR of 2.5–3.5 has been recommended for mechanical prosthetic heart valves and prevention of recurrent systemic emboli. If PT is monitored, it should be 1.5–2 times the control. Patients at high risk for bleeding may benefit from more frequent INR monitoring. Onset of action occurs within 36–72 hr, and peak effects occur within 5–7 days. IV dosing is equivalent to PO doses and is used in situations where oral dosing is not possible. **The antidote is vitamin K and fresh frozen plasma.**

**ZAFIRLUKAST**

Accolate and generics

**Anti-asthmatic, leukotriene receptor antagonist**

Yes



No



3



B

**Tabs:** 10, 20 mg**Asthma:****Child 5–11 yr:** 10 mg PO BID**Child ≥ 12 yr and adult:** 20 mg PO BID

Contraindicated in hepatic impairment, including hepatic cirrhosis. May cause headache, dizziness, nausea, diarrhea, abdominal pain, vomiting, generalized pain, asthenia, myalgia, fever, LFT elevation, and dyspepsia. Eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy have been reported, primarily in patients with oral steroid dose reduction. Hepatitis, hyperbilirubinemia, hepatic failure, hypersensitivity reactions (e.g., urticaria, angioedema and rashes), and neuropsychiatric events (e.g., aggression, anxiety, dream abnormalities, hallucinations, depression, suicidal behavior, insomnia) have also been reported.



Drug is a substrate for CYP 450 2C9 and inhibits CYP 450 2C9 and 3A4 isoenzymes. Erythromycin, terfenadine, and theophylline decrease zafirlukast levels; aspirin increases levels. Zafirlukast may increase effects of warfarin. Administer doses on an empty stomach, at least 1 hr before or 2 hr after eating.

**ZIDOVUDINE**

Retrovir, AZT, and generics

**Antiviral agent, nucleoside analog reverse transcriptase inhibitor**

Yes



Yes



3



C

**Caps:** 100 mg**Tabs:** 300 mg**Oral syrup:** 50 mg/5 mL (240 mL); contains 0.2% sodium benzoate**Injection:** 10 mg/mL (20 mL); preservative free**In combination with lamivudine (3TC) as Combivir:****Tabs:** 300 mg zidovudine + 150 mg lamivudine**In combination with abacavir and lamivudine (3TC) as Trizivir:****Tabs:** 300 mg zidovudine + 300 mg abacavir + 150 mg lamivudine**HIV:** See [www.aidsinfo.nih.gov/guidelines](http://www.aidsinfo.nih.gov/guidelines).**Prevention of vertical transmission:****14–34 weeks of pregnancy (maternal dosing):****Until labor:** 600 mg/24 hr PO ÷ BID–TID**During labor:** 2 mg/kg/dose IV over 1 hr, followed by 1 mg/kg/hr IV infusion until umbilical cord clamped**Term neonate and infant < 6 wk (initiate therapy within 12 hr of birth and continue until 6 wk' of age):****PO:** 2 mg/kg/dose Q6 hr or 4 mg/kg/dose Q12 hr**IV:** 1.5 mg/kg/dose Q6 hr or 3 mg/kg/dose Q12 hr, administered over 60 min

ZIDOVUDINE *continued***Premature infant:**

Gestational Age (wk)	Oral (PO) Dosage	Intravenous (IV) Dosage*
<30	2 mg/kg/dose Q12 hr; increase to 3 mg/kg/dose Q12 hr at 4 wk of age	1.5 mg/kg/dose Q12 hr; increase to 2.3 mg/kg/dose Q12 hr at 4 wk of age
30–34	2 mg/kg/dose Q12 hr; increase to 3 mg/kg/dose Q12 hr at postnatal age of 15 days	1.5 mg/kg/dose Q12 hr; increase to 2.3 mg/kg/dose Q12 hr at postnatal age of 15 days
≥35	4 mg/kg/dose Q12 hr	3 mg/kg/dose Q12 hr

\*Convert to PO route when possible.

**HIV postexposure prophylaxis (all therapies to begin within 2 hr of exposure if possible):**

≥ 12 yr and adult: 200 mg/dose PO TID or 300 mg/dose PO BID × 28 days. Use in combination with lamivudine or emtricitabine and with either one of the following: lopinavir/ritonavir, atazanavir/ritonavir, darunavir/ritonavir, raltegravir, etravirine, or etravirine × 28 days. Many other regimens exist; see [www.aidsinfo.nih.gov/guidelines](http://www.aidsinfo.nih.gov/guidelines) for the most recent information.

See [www.aidsinfo.nih.gov/guidelines](http://www.aidsinfo.nih.gov/guidelines) for additional remarks.

**Use with caution** in patients with impaired renal or hepatic function. Dosage reduction is recommended in severe renal impairment and may be necessary in hepatic dysfunction. Drug penetrates well into CNS. Most common side effects include anemia, granulocytopenia, nausea, and headache (dosage reduction, erythropoietin, filgrastim/G-CSF, or discontinuance may be required, depending on event). Seizures, confusion, rash, myositis, myopathy (use > 1 yr), hepatitis, and elevated liver enzymes have been reported. Macrocytosis is noted after 4 wk of therapy and can be used as an indicator of compliance. Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported.

**Do not use** in combination with stavudine because of poor antiretroviral effect. Effects of interacting drugs include increased toxicity (acyclovir, trimethoprim-sulfamethoxazole), increased hematologic toxicity (ganciclovir, interferon- $\alpha$ , marrow-suppressive drugs), and granulocytopenia (drugs that affect glucuronidation). Methadone, atovaquone, cimetidine, valproic acid, probenecid, and fluconazole may increase levels of zidovudine. Rifampin, rifabutin, and clarithromycin may decrease levels.

**Do not administer IM.** IV form is incompatible with blood product infusions and should be infused over 1 hr (intermittent IV dosing). Despite manufacturer recommendations of administering oral doses 30 min before or 1 hr after meals, doses may be administered with food.

**ZINC SALTS, SYSTEMIC**

Galzin, Orazinc, and other generics

**Trace mineral**

No



No



3



A/C

**Tabs as sulfate (Orazinc and generics) [OTC], 23% elemental:** 50, 66, 110, 220 mg

**Caps as sulfate (Orazinc, and generics) [OTC], 23% elemental:** 220 mg

**Caps as acetate (Galzin):** 25, 50 mg elemental per capsule

**Liquid as acetate:** 5 mg elemental Zn/mL

**Liquid as sulfate:** 10 mg elemental Zn/mL

**Injection as sulfate:** 1 mg elemental Zn/mL (10 mL), 5 mg elemental Zn/mL (5 mL); may contain benzyl alcohol

**Injection as chloride:** 1 mg elemental Zn/mL (10 mL)

*Continued*



ZINC SALTS, SYSTEMIC *continued***Zinc deficiency (see remarks):****Infant and child:** 0.5–1 mg elemental Zn/kg/24 hr PO ÷ once daily–TID**Adult:** 25–50 mg elemental Zn/dose (100–220 mg Zn sulfate/dose) PO TID**Wilson disease:****Child ( $\geq 10$  yr):** 75 mg/24 hr elemental Zn PO ÷ TID. If needed, may increase to 150 mg/24 hr elemental Zn PO ÷ TID.**U.S. RDA:** See Chapter 21.

For supplementation in parenteral nutrition, see Chapter 21.

Nausea, vomiting, GI disturbances, leukopenia, and diaphoresis may occur. Gastric ulcers, hypotension, and tachycardia may occur at high doses. Patients with excessive losses (burns) or impaired absorption require higher doses. Therapeutic levels: 70–130 mcg/dL.

May decrease absorption of penicillamine, tetracycline, and fluoroquinolones (e.g., ciprofloxacin). Drugs that increase gastric pH (e.g., H<sub>2</sub> antagonists and proton pump inhibitors) can reduce zinc absorption. Excessive zinc administration can cause copper deficiency.

Approximately 20%–30% of oral dose is absorbed. Oral doses may be administered with food if GI upset occurs. Pregnancy category is "A" for zinc acetate and "C" for all other salt forms.

**ZONISAMIDE**

Zonegran and generics

**Anticonvulsant**

Yes



Yes



2



C

**Caps:** 25, 50, 100 mg**Oral syrup:** 10 mg/mL **Infant and child (data incomplete):**

**Suggested dosing from a review of Japanese open-label studies for partial and generalized seizures:** Start with 1–2 mg/kg/24 hr PO ÷ BID. Increase dosage by 0.5–1 mg/kg/24 hr Q2 wk to usual dosage range of 5–8 mg/kg/24 hr PO ÷ BID.

**Recommended higher alternative dosing:** Start with 2–4 mg/kg/24 hr PO ÷ BID–TID. Gradually increase dosage at 1- to 2-wk intervals to 4–8 mg/kg/24 hr. **Max. dose:** 12 mg/kg/24 hr.

**Infantile spasms (regimen that was effective in a small study from Japan; additional studies are needed):** Start with 2–4 mg/kg/24 hr PO ÷ BID. Then increase by 2–5 mg/kg/24 hr every 2–4 day until seizures disappear, up to a **max.** of 20 mg/kg/24 hr.

**>16 yr–adult:**

**Adjunctive therapy for partial seizures:** 100 mg PO once daily  $\times$  2 wk. Dose may be increased to 200 mg PO once daily  $\times$  2 wk. Additional dosage increments of 100 mg/24 hr can be made at 2-wk intervals to allow attainment of steady-state levels. Effective doses have ranged from 100–600 mg/24 hr ÷ once daily–BID (BID dosing may provide better efficacy). No additional benefit has been shown for doses  $>400$  mg/24 hr.

Because zonisamide is a sulfonamide, it is **contraindicated** in patients allergic to sulfonamides (may result in Stevens-Johnson syndrome or TEN). Common side effects of drowsiness, ataxia, anorexia, GI discomfort, headache, rash, and pruritus usually occur early in therapy and can be minimized with slow dose titration. Urolithiasis and metabolic acidosis (more frequent and severe in younger patients) have been reported. Children are at increased risk for hyperthermia and oligohydrosis, especially in warm or hot weather. Suicidal behavior or ideation, acute pancreatitis, rhabdomyolysis, and elevated creatinine phosphokinase have been reported.

*Continued*

ZONISAMIDE *continued*

Although not fully delineated, therapeutic serum levels of 20–30 mg/L have been suggested because higher rates of adverse reactions have been seen at levels >30 mg/L.

Zonisamide is a CYP P450 3A4 substrate. Phenytoin, carbamazepine, and phenobarbital can decrease levels of zonisamide.

**Use with caution** in renal or hepatic impairment; slower dose titration and more frequent monitoring is recommended. **Do not use** if GFR is <50 mL/min. **Avoid** abrupt discontinuation or radical dose reductions. Swallow capsules whole, and **do not** crush or chew.

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# Chapter 30

## Formulary Adjunct

*Sara Mixter, MD, MPH, and  
J. Deanna Wilson, MD*

Special thanks go to the following people who provided guidance in preparing the elements of Chapter 30 in past editions: Sande Okelo, MD; Allison Kirk, MD; Bernard Cohen, MD; Katherine Puttgen, MD; Amy Schwartz, RD; Michael Repka, MD; Elizabeth Shumann, MD; Alix Dabb, Pharm D.

### I. WEBSITES

Physician's Desk Reference: <http://www.pdr.net/Default.aspx>

Lexi-Comp Drug Reference: <http://online.lexi.com>

G6PD Deficiency: <http://g6pddeficiency.org/index.php?cmd=contraindicated>

### II. SYSTEMIC CORTICOSTEROIDS

- A. Body surface area nomogram and equation for calculating steroid dose (Fig. 30-1)
- B. Potency of various therapeutic steroids content moved to Chapter 10, Endocrinology

### III. INHALED CORTICOSTEROIDS FOR AIRWAY INFLAMMATION

Content moved to Chapter 24, Pulmonology

### IV. TOPICAL CORTICOSTEROIDS

Content moved to Chapter 8, Dermatology

### V. COMMON INSULIN FORMULATIONS

Content moved to Chapter 10, Endocrinology

### VI. PANCREATIC ENZYME SUPPLEMENTS

See Table 30-1

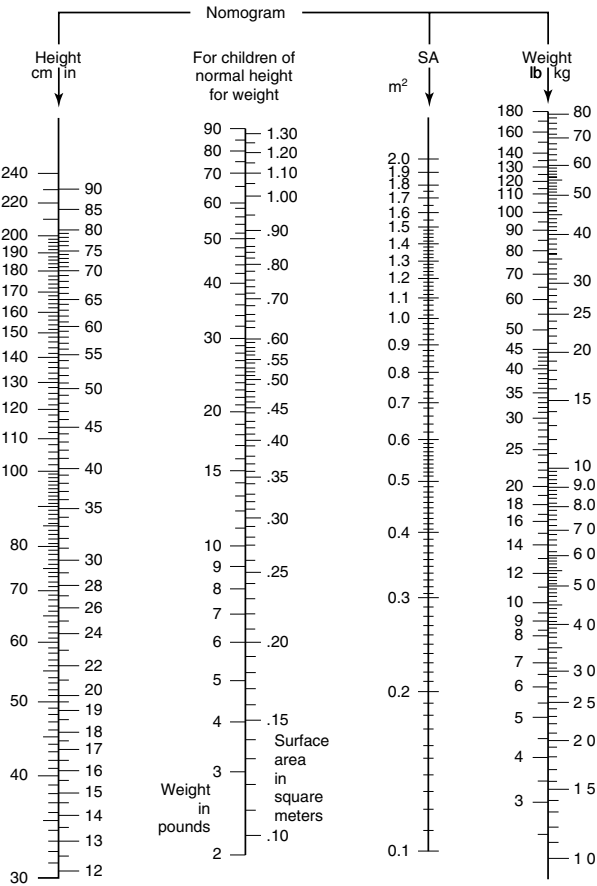
### VII. COMMON INDUCERS AND INHIBITORS OF THE CYTOCHROME P450 SYSTEM

Table 30-2 is meant to give some common pediatric examples of inducers/inhibitors. Other resources have more complete listings.<sup>1</sup>

### VIII. OPHTHALMIC DRUGS

A. See Table 30-3

B. Content on treating allergic conjunctivitis moved to Chapter 15, Immunology and Allergy



Alternative (Mosteller's formula):

$$\text{Surface area (m}^2\text{)} = \sqrt{\frac{\text{Height (cm)} \times \text{Weight (kg)}}{3600}}$$

**FIGURE 30-1** Body surface area nomogram and equation. (From Briars GL, Bailey BJ. Surface area estimation: pocket calculator V nomogram. Arch Dis Child. 1994;70:246-247.)

TABLE 30-1

## PANCRELIPASE\*

Product	Lipase (USP) Units	Amylase (USP) Units	Protease (USP) Units
Creon			
6	6000	30,000	19,000
12	12,000	60,000	38,000
24	24,000	120,000	76,000
Pancreaze MT			
4	4200	17,500	10,000
10	10,500	43,750	25,000
16	16,800	70,000	40,000
20	21,000	61,000	37,000
Zenpep			
5	5000	27,000	17,000
10	10,000	55,000	34,000
15	15,000	82,000	51,000
20	20,000	109,000	68,000

\*See Formulary for side effects associated with administration. As of April 12, 2010, these are the only three products approved by the U.S. Food and Drug Administration (FDA). Many were recently removed from the market. Products are all supplied as delayed-release capsules.

<http://www.zenpep.com/site/cfpatient.aspx>

<http://newdrugreview.com/index.php/gastrointestinal-drugs/pancreaze-3-dosage-forms-and-strengths>

U.S. Food and Drug Administration: Updated questions and answers for healthcare professionals and the public: use an approved pancreatic enzyme product (PEP). Accessed August 11, 2010.

<http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm204745.htm>

Data from <http://www.creon-us.com/Healthcare-Professional/default.htm>.

TABLE 30-2

## EXAMPLES OF INDUCERS AND INHIBITORS OF CYTOCHROME P450 SYSTEM

Isoenzyme	Substrates (Drugs Metabolized by Isoenzyme)	Inhibitors*	Inducers
CYP1A2	Caffeine, theophylline, estradiol, propranolol	Cimetidine, quinolones, fluvoxamine, ketoconazole, lidocaine	Carbamazepine, smoking, phenobarbital, rifampin
CYP2B6	Cyclophosphamide, efavirenz, propofol	Paroxetine, sertraline	Carbamazepine, (fos)phenytoin, phenobarbital, rifampin
CYP2C9/10	Warfarin, phenytoin, tolbutamide, fluoxetine, sulfamethoxazole, fosphenytoin	Amiodarone, fluconazole, ibuprofen, indomethacin, nicardipine	Carbamazepine, (fos)phenytoin, rifampin, phenobarbital
CYP2C19	Diazepam, PPIs, phenytoin, desogestrel, ifosfamide, phenobarbital, sertraline	Cimetidine fluvoxamine, fluconazole, isoniazid, PPIs, sertraline	Carbamazepine, (fos)phenytoin, rifampin

*Continued*

TABLE 30-2

## EXAMPLES OF INDUCERS AND INHIBITORS OF CYTOCHROME P450 SYSTEM (Continued)

Isoenzyme	Substrates (Drugs Metabolized by Isoenzyme)	Inhibitors*	Inducers
CYP2D6	Captopril, codeine, haloperidol, dextromethorphan, tricyclic antidepressants, hydrocodone, oxycodone, phenothiazines, metoprolol, propranolol, paroxetine, venlafaxine, risperidone, flecainide, sertraline, aripiprazole, fluoxetine, lidocaine, fosphenytoin, ritonavir	Chlorpromazine, cinacalcet, dexmedetomidine, cocaine, cimetidine, quinidine, ritonavir, fluoxetine, sertraline, amiodarone	None known
CYP2E1	Acetaminophen, alcohol, isoniazid, theophylline, isoflurane	Disulfiram	Alcohol
CYP3A4	Amlodipine, aripiprazole, budesonide, cocaine, clonazepam, diltiazem, efavirenz, erythromycin, estradiol, fentanyl, fluticasone, nifedipine, verapamil, cyclosporine, carbamazepine, cisapride, tacrolimus, midazolam, alfentanil, diazepam, ifosfamide, imatinib, itraconazole, ketoconazole, cyclophosphamide, PPIs, haloperidol, lidocaine, medroxyprogesterone, methadone, methylprednisolone, salmeterol, theophylline, quetiapine, ritonavir, indinavir, sildenafil	Erythromycin, cimetidine, clarithromycin, isoniazid, ketoconazole, itraconazole, metronidazole, sertraline, ritonavir, indinavir, imatinib, nicardipine, propofol, quinidine	Rifampin, (fos) phenytoin, phenobarbital, carbamazepine, dexamethasone

\*Only strong and some moderate inhibitors are listed here. Weak inhibitors also exist.

**NOTE:** The cytochrome P450 enzyme system is composed of different isoenzymes. Each isoenzyme metabolizes a unique group of drugs or substrates. When an *inhibitor* of a particular isoenzyme is introduced, the serum concentration of any drug or *substrate* metabolized by that particular isoenzyme will *increase*. When an *inducer* of a particular isoenzyme is introduced, the serum concentration of drugs or *substrates* metabolized by that particular isoenzyme will *decrease*.

CYP, Cytochrome P450; PPI, proton pump inhibitor.

Data from Taketomo CK, Hodding JH, Kraus DM. *American Pharmaceutical Association Pediatric Dosage Handbook*. 16th ed. Hudson, OH: Lexi-Comp, 2009; Zevin S, Benowitz NL. Drug interactions with tobacco smoking. An update. *Clin Pharmacokinet*. 1999;36:425-438; Cupp MJ, Tracy TS. Cytochrome P450: new nomenclature and clinical implications. *Am Fam Physician*. 1998;57:107-116.

TABLE 30-3

## OPHTHALMIC DRUGS

Brand Name	Ingredient	Indication	Dose
Alomide (>2 yr) Sol: 10 mL	Lodoxamide tromethamine 0.1% (mast cell stabilizer)	Vernal conjunctivitis and keratitis, keratoconjunctivitis	1–2 gtt QID up to 3 mo
Azasite (≥1 yr) Sol: 2.5 mL	Azithromycin 1% (contains benzalkonium chloride)	Conjunctivitis	1 gtt BID × 2 days, then Q day × 5 days
Bleph-10 (>2 mo) Sol: 2.5 mL, 5 mL, 15 mL Oint: 3.5 g	Sulfacetamide sodium 10% Sol: Benzalkonium chloride Oint: phenylmercuric acetate	Conjunctivitis Ophthalmic solution used as adjunct in trachoma	1–2 gtt Q2–3 hr or small amount of oint Q3–4 hr for 7–10 days Trachoma: 2 gtt Q2 hr w/systemic therapy
Cortisporin Oph susp: 7.5 mL Oph oint: 3.5 g	Susp (per mL): Polymyxin B sulfate (10,000 U), neomycin sulfate (0.35%), hydrocortisone (1%) Oint (per g): Polymyxin B sulfate (10,000 U), neomycin sulfate (0.35%), bacitracin zinc (400 U), hydrocortisone (1%)	Ocular inflammation associated with infection <b>Contraindicated in fungal, viral, or mycobacterial infection</b> Use with caution in glaucoma or in corneal or scleral thinning	1–2 gtt or small amount of oint TID–QID
Erythromycin Oint: 1, 3.5 g	Erythromycin (5 mg/g)	Conjunctivitis Prophylaxis of ophthalmia neonatorum	Small amount up to 6 times daily 0.5–1 cm to each conjunctival sac
Neosporin Oint: 3.75 g Sol: 10 mL	Oint (per g): Polymyxin B sulfate (10,000 U), bacitracin zinc (400 U), neomycin sulfate (3.5 mg) Sol (per mL): Polymyxin B sulfate (10,000 U), neomycin sulfate (1.75 mg), gramicidin (0.025 mg), 0.5% alcohol	Conjunctivitis	1–2 gtt or small amount of oint Q4 hr for 7–10 days For acute infections, 1–2 gtt 2–4 × Q1 hr initially
Ocuflox (>1 yr) Sol: 5 mL, 10 mL	Ofloxacin 0.3%, benzalkonium chloride	Conjunctivitis Corneal ulcer	1–2 gtt Q2–4 hr × 2 days, then QID × 5 days 1–2 gtt Q30 min while awake; at 4 hr and 6 hr during sleep × 2 days; then 1–2 gtt Q1 hr while awake × 5–7 days, then QID until treatment completion

Continued



TABLE 30-3

## OPHTHALMIC DRUGS (Continued)

Brand Name	Ingredient	Indication	Dose
Poly-Pred Susp: 5 mL, 10 mL	Susp (per mL): Prednisolone acetate (0.5%), neomycin sulfate (0.35%), polymyxin B sulfate (10,000 U)	Ocular inflammation associated with infection  <b>Contraindicated in fungal, viral, or mycobacterial infections</b>  Use with caution in glaucoma or in corneal or scleral thinning	1–2 gtt Q3–4 hr
Polysporin Oint: 3.5 g	Oint (per g): Polymyxin B sulfate (10,000 U), bacitracin zinc (500 U)	Conjunctivitis	1–2 gtt Q3–4 hr; do not use >7 days
Polytrim (>2 mo) Sol: 10 mL	Trimethoprim sulfate (1 mg), polymyxin B sulfate (10,000 U/mL), benzalkonium chloride	Conjunctivitis	1 gtt Q3 hr × 7–10 days
Pred-Forte Sol: 1, 5, 10, 15 mL Pred-Mild Sol: 5, 10 mL	Prednisolone acetate 1% Prednisolone acetate 0.12%	Ocular/conjunctival inflammation.  <b>Contraindicated in fungal, viral, or mycobacterial infections</b>  Prolonged use may cause glaucoma, corneal/scleral thinning	1–2 gtt 2–4 × per day Safety and efficacy not established in children
Tobrex Sol: 5 mL Oint: 3.5 g	Sol: Tobramycin 0.3%, benzalkonium chloride Oint: Tobramycin 0.3%, chlorobutanol	Conjunctivitis	Severe infections: 2 gtt Q1 hr or ½ inch of ointment Q3–4 hr Mild–moderate infections: 1–2 gtt Q4 hr or ½ inch of ointment BID–TID
Vigamox (≥1 yr) Sol: 3 mL	Moxifloxacin hydrochloride 0.5% (fluoroquinolone)	Bacterial conjunctivitis	1 gtt TID × 7 days
Viroptic (>6 yr) Sol: 7.5 mL	Trifluridine 1%, contains thimerosal	Primary keratocon- junctivitis, recurrent epithelial keratitis due to herpes simplex virus 1 and 2	1 gtt Q2 hr while awake (maximum 9 gtt/day) 1 gtt Q4 hr × 7 days after re-epithelialization (maximum 21 days)
Zymar (≥1 yr) Sol: 5 mL	Gatifloxacin 0.3% (fluoro- quinolone)	Bacterial conjunctivitis	1 gtt Q2 hr while awake, up to 8 times/ day × 2 days; then 1 gtt up to QID × 5 days

Modified from *Physician's Desk Reference*. 64th ed. Montvale, NJ: Medical Economics, 2010.

**IX. PSYCHIATRIC DRUG FORMULARY**

Content moved to Chapter 9, Development, Behavior, and Mental Health

**X. CHEMOTHERAPEUTIC AGENTS**

Content moved to Chapter 22, Oncology

**XI. OXIDIZING AGENTS AND GLUCOSE-6-PHOSPHATE  
DEHYDROGENASE (G6PD) DEFICIENCY**

A comprehensive listing of relevant drugs is available at:

<http://g6pddeficiency.org/index.php?cmd=contraindicated>

**REFERENCE**

1. Taketomo CK, Hodding JH, Kraus DM. *American Pharmaceutical Association Pediatric Dosage Handbook*. 16th ed. Hudson, OH: Lexi-Comp, 2009.

# Chapter 31

## Drugs in Renal Failure

*Monica C. Mix, MD, and Branden Engorn, MD*

### I. DOSE ADJUSTMENT METHODS

#### A. Maintenance Dose

In patients with renal insufficiency, the dose may be adjusted using the following methods:

1. **Interval extension (I):** Lengthen intervals between individual doses, keeping dose size normal. For this method, suggested interval is shown.
2. **Dose reduction (D):** Reduce amount of individual doses, keeping interval between doses normal; recommended when a relatively constant blood level of drug is desired. For this method, percentage of usual dose is shown.
3. **Interval extension and dose reduction (DI):** Both lengthen interval and reduce dose.
4. **Interval extension or dose reduction (D, I):** In some instances, either dose or interval can be changed.

**NOTE:** These dose adjustment methods apply only to patients beyond the neonatal period. For neonatal renal dosing, please consult a neonatal dosage reference. Dose modifications given are only approximations.

**Each patient must be monitored closely for signs of drug toxicity, and serum levels must be measured when available; drug dose and interval should be adjusted accordingly.** When in doubt, always consult a nephrologist or pharmacist who has expertise in renal dosing.

#### B. Dialysis

Quantitative effects of hemodialysis (He) and peritoneal dialysis (P) on drug removal are shown. "Y" indicates necessity for a supplemental dose with dialysis (in some cases, supplemental dose may not be a full dose). "N" indicates no need for adjustment. The designation "No" does not preclude use of dialysis or hemoperfusion for drug overdose. The "?" indicates insufficient data available. **Please consult with a nephrologist or pharmacist who is very familiar with renal dosing in dialysis.**

### II. ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE (TABLE 31-1)

### III. NON-ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE (TABLE 31-2)

TABLE 31-1

ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE<sup>1-4</sup>

Drug	Route of Excretion*	Pharmacokinetics		Adjustments in Renal Failure				Supplemental Dose for Dialysis
		Normal $t_{1/2}$ (hr)	Normal Dose Interval	Method	CrCl (mL/min)	Dose	Interval	
Acyclovir (IV)	Renal	2–4	Q8 hr	D, I	25–50	NI	Q12 hr	Y (He)
					10–25	NI	Q24 hr	N (P)
					<10	50% ↓	Q24 hr	
Amantadine†	Renal	10–28	Q12–24 hr	D, I	30–50	50% ↓	Q24 hr	N (He)α
					15–29	50% ↓	Q48 hr	N (P)
					<15	NI daily dose	Q7 days	
Amikacin	Renal	1.5–3	Q8–12 hr	I	Loading dose 5–7.5 mg/kg; subsequent doses are best determined by serum levels and assessment of renal insufficiency. <sup>1</sup>			Y (He) Y (P)
Amoxicillin‡	Renal	0.7–2	Q8–12 hr	I	10–50	NI	Q12 hr	Y (He)
					<10	NI	Q24 hr	N (P)
Amoxicillin/clavulanate‡	Renal	1	Q8–12 hr	I	10–30	NI	Q12 hr	Y (He)
					<10	NI	Q24 hr	N (P)
Amphotericin B	Renal (40% over 7 days)	Initial 15–48 hr Terminal 15 days	Q24 hr	D, I	Dosage adjustments are unnecessary with preexisting renal impairment. If decreased renal function is due to amphotericin B, daily dose can be decreased by 50%, or dose given every other day. <sup>1</sup>			N (He) N (P)
Amphotericin B lipid complex (Abelcet)	Renal (1%)	173	Q24 hr		No guidelines established.			N (He) N (P)
Amphotericin B, liposomal (AmBisome)	Renal (≤10%)	100–153	Q24 hr		No guidelines established.			N (He) N (P)
Ampicillin†	Renal	1–4	Q6–12 hr	I	10–50	NI	Q6–12 hr	Y (He)
					<10	NI	Q12 hr	? (P)

TABLE 31-1

## ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE (Continued)

Drug	Route of Excretion*	Pharmacokinetics		Adjustments in Renal Failure				
		Normal $t_{1/2}$ (hr)	Normal Dose Interval	Method	CrCl (mL/min)	Dose	Interval	Supplemental Dose for Dialysis
Ampicillin/sulbactam	Renal	1–1.8	Q4–6 hr	I	15–29 <15	NI NI	Q12 hr Q24 hr	Y (He) ? (P)
Aztreonam	Renal (hepatic)	1.3–2.2	Q6–12 hr	D	10–30 <10	50% ↓ 75% ↓	NI NI	Y (He) Y (P)
Cefaclor	Renal	0.5–1	Q8–12 hr	D	<10	50% ↓	NI	Y (He) ? (P)
Cefadroxil	Renal	1–2	Q12 hr	I	10–50 <10	NI NI	Q24 hr Q36 hr	Y (He) Y (P)
Cefazolin	Renal	1.5–2.5	Q6–8 hr	D, I	35–54 11–34 <10	NI 50% ↓ <sup>Σ</sup> 50% ↓ <sup>Σ</sup>	Q8 hr Q12 hr Q18–24 hr	Y (He) N (P)
<b>Note:</b> Give initial loading dose, then adjust subsequent doses for renal function.								
Cefdinir	Renal	1.1–2.3	Q12–24 hr	D, I	<30	7 mg/kg/dose (children; max 300 mg) He	Q24 hr Q48 hr	Y (He) <sup>Ω</sup> ? (P)
Cefepime <sup>†</sup>	Renal	1.8–2	Q8–12 hr	D, I	10–50 <10	NI 50% ↓	Q24 hr Q24 hr	Y (He) ? (P)

TABLE 31-1

## ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE (Continued)

Drug	Pharmacokinetics			Adjustments in Renal Failure				
	Route of Excretion*	Normal $t_{1/2}$ (hr)	Normal Dose Interval	Method	CrCl (mL/min)	Dose	Interval	Supplemental Dose for Dialysis
Cefixime	Renal (hepatic)	3–4	Q12–24 hr	D	21–60 <20	25% ↓ 50% ↓	NI NI	Y (He) ? (P)
Cefotaxime	Renal	1–3.5	Q6–12 hr	D	<20	50% ↓	NI	Y (He) ? (P)
Cefotetan	Renal (hepatic)	3.5	Q12 hr	I	10–30 <10	NI NI	Q24 hr Q48 hr	Y (He) ? (P)
Cefoxitin	Renal	0.75–1.5	Q4–8 hr	I	30–50 10–30 <10	NI NI NI	Q8–12 hr Q12–24 hr Q24–48 hr	Y (He) ? (P)
Cefpodoxime	Renal	2.2	Q12 hr	I	<30	NI	Q24 hr	Y (He) <sup>§</sup> N (P)
Cefprozil	Renal	1.3	Q12–24 hr	D	<30	50% ↓	NI	Y (He) ? (P)
Ceftazidime	Renal	1–2	Q8–12 hr	I	30–50 10–30 <10	NI NI NI	Q12 hr Q24 hr Q24–48 hr	Y (He) ? (P)
Ceftibuten	Renal	1.5–2.5	Q24 hr	D	30–49 5–29	50% ↓ 75% ↓	NI NI	Y (He) <sup>αα</sup> ? (P)
Cefuroxime (IV)	Renal	1.6–2.2	Q8–12 hr	I	10–20 <10	NI NI	Q12 hr Q24 hr	Y (He) ? (P)
Cephalexin	Renal	0.5–1.2	Q6–8 hr	I	10–40 <10	NI NI	Q8–12 hr Q12–24 hr	Y (He) ? (P)

Continued

TABLE 31-1

## ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE (Continued)

Drug	Pharmacokinetics			Adjustments in Renal Failure				Supplemental Dose for Dialysis
	Route of Excretion*	Normal t <sub>1/2</sub> (hr)	Normal Dose Interval	Method	CrCl (mL/min)	Dose	Interval	
Ciprofloxacin <sup>†</sup>	Renal (hepatic)	1.2–5	Q8–12 hr	D, I	<30 (IV) 30–50 (PO) <30 (PO)	200–400 mg <sup>†</sup> 250–500 mg <sup>†</sup> 250–500 mg <sup>†</sup>	Q18–24 hr Q12 hr Q18 hr	Y (He) ? (P)
Clarithromycin	Renal (hepatic)	3–7	Q12 hr	D, I	<30	50% ↓	Q12–24 hr	? (He) ? (P)
Ertapenem <sup>†</sup>	Renal (hepatic)	4	Q12–24 hr	D	≤30	50% ↓	NI	Y (He) ? (P)
Erythromycin	Hepatic (renal)	1.5–2	Q6–12 hr	D	<10	25%–50%↓	NI	N (He) N (P)
Ethambutol	Renal (hepatic)	2.5–3.6	Q24 hr	I	10–50 <10	NI NI	Q24–36 hr Q48 hr	Y (He) ? (P)
Famciclovir <sup>†</sup>	Renal (hepatic)	2–3	Q8 hr	D, I	Herpes Zoster Treatment <sup>†,***</sup> 40–59 500 mg 20–39 500 mg <20 250 mg Recurrent Genital Herpes Treatment <sup>†,***</sup> 40–59 500 mg 20–39 500 mg <20 250 mg Recurrent Genital Herpes Suppression <sup>†,ΣΣ</sup> >40 250 mg 20–39 125 mg <20 125 mg		Q12 hr Q24 hr Q24 hr Q12 hr × 1 day Single dose Single dose Q12 hr Q12 hr Q24 hr	Y (He) ? (P)

TABLE 31-1

## ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE (Continued)

Drug	Pharmacokinetics			Adjustments in Renal Failure				Supplemental Dose for Dialysis
	Route of Excretion*	Normal t <sub>1/2</sub> (hr)	Normal Dose Interval	Method	CrCl (mL/min)	Dose	Interval	
					Recurrent Herpes Labialis—Single Dose Regimen†,***			
					>60	1500 mg as single dose		
					40–59	750 mg as single dose		
					20–39	500 mg as single dose		
					<20	250 mg as single dose		
					Recurrent Orolabial or Genital Herpes in HIV-Infected Patients†,***			
					40–59	500 mg	Q12 hr	
					20–39	500 mg	Q12 hr	
					<20	250 mg	Q24 hr	
					Fluconazole†	Renal	19–25	Q24 hr
Flucytosine	Renal	3–8	Q6 hr	I	20–40	NI	Q12 hr	Y (He)
					10–20	NI	Q24 hr	Y(P)
					<10	NI	Q24–48 hr	
Foscarnet	Renal	2–4.5	Induct: Q8 hr Maint: Q24 hr	D	See package insert for adjustments for induction and maintenance.			? (He) ? (P)
Ganciclovir	Renal	2.5–3.6	Induct: Q12 hr IV  Maint: Q24 hr IV/PO OR Q8 hr	D, I	Induction IV			Y (He)§ N (P)
					50–69	2.5 mg/kg	Q12 hr	
					25–49	2.5 mg/kg	Q24 hr	
					10–24	1.25 mg/kg	Q24 hr	
					<10	1.25 mg/kg	3 times/wk after He	

Continued



TABLE 31-1

## ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE (Continued)

Drug	Pharmacokinetics			Adjustments in Renal Failure					
	Route of Excretion <sup>*</sup>	Normal t <sub>1/2</sub> (hr)	Normal Dose Interval	Method	CrCl (mL/min)	Dose	Interval	Supplemental Dose for Dialysis	
Gentamicin <sup>†</sup>	Renal	1.5–3	Q8–12 hr	I	Maintenance IV				
					50–69	2.5 mg/kg	Q24 hr	Y (He) Y (P) <sup>†</sup>	
					25–49	1.25 mg/kg	Q24 hr		
					10–24	0.625 mg/kg	Q24 hr		
					<10	0.625 mg/kg	3 times/wk after He		
					Maintenance PO <sup>†</sup>				
					50–69	1500 mg	Q24 hr		
						OR 500 mg	Q8 hr		
					25–49	1000 mg	Q24 hr		
						OR 500 mg	Q12 hr		
					10–24	500 mg	Q24 hr		
					<10	500 mg	3 times/wk after He		
					>50	NI	NI		
					<50	Give usual initial dose and monitor levels.			

TABLE 31-1

## ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE (Continued)

Drug	Route of Excretion*	Pharmacokinetics		Adjustments in Renal Failure				Supplemental Dose for Dialysis
		Normal $t_{1/2}$ (hr)	Normal Dose Interval	Method	CrCl (mL/min)	Dose	Interval	
Imipenem/cilastatin	Renal	1–1.4	Q6–8 hr	D, I	41–70	50% ↓	Q6 hr	Y (He) ? (P)
					21–40	63% ↓	Q8 hr	
					6–20	75% ↓ in max daily dose	Q12 hr	
					≤5	Should not receive imipenem unless on hemodialysis		
Kanamycin	Renal	2–3	Q8 hr	I	>50	NI	Q12 hr	Y (He) Y (P)
					10–50	NI	Q12–18 hr	
					<10	NI	Q24–48 hr	
Lamivudine†, **	Renal	1.7–2.5	Q12 hr	D, I	30–49	NI	Q24 hr	N (He)
					15–29	First dose 100%, then 66%	Q24 hr	N (P)
					5–14	First dose 100%, then 33%	Q24 hr	
					<5	First dose 33%, then 17%	Q24 hr	

Continued

TABLE 31-1

## ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE (Continued)

Drug	Route of Excretion*	Pharmacokinetics		Adjustments in Renal Failure				Supplemental Dose for Dialysis
		Normal $t_{1/2}$ (hr)	Normal Dose Interval	Method	CrCl (mL/min)	Dose	Interval	
Levofloxacin†	Renal (hepatic)	6–8	Q12–24 hr	D, I	<b>500-mg Q24-hr Regimen</b>			N (He) N (P)
					20–49	First dose 500 mg, then 250 mg	Q24 hr	
					10–19	First dose 250–500 mg, then 250 mg	Q48 hr	
					<b>750-mg Q24-hr Regimen</b>			
					20–49	750 mg	Q48 hr	
					10–19	500 mg	Q48 hr	
					<b>250-mg Q24-hr Regimen</b>			
					10–19	250 mg	Q48 hr	
Meropenem	Renal	1–1.5	Q8 hr	D, I	26–50	NI	Q12 hr	Y (He)
					10–25	50% ↓	Q12 hr	? (P)
					<10	50% ↓	Q24 hr	
Metronidazole	Hepatic (renal)	6–12	Q6–12 hr	D	<10	50% ↓	NI	Y (He) Y (P)

TABLE 31-1

## ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE (Continued)

Drug	Route of Excretion*	Pharmacokinetics		Method	Adjustments in Renal Failure			
		Normal $t_{1/2}$ (hr)	Normal Dose Interval		CrCl (mL/min)	Dose	Interval	Supplemental Dose for Dialysis
Norfloxacin	Hepatic (renal)	3–4	Q12 hr	I	10–50	NI	Q12–24 hr	N (He)
					<10	NI	Q24 hr	N (P)
Oseltamivir†	Renal	1–10	Q12–24 hr	I	<b>Influenza Treatment</b>			Y (He)
					10–30	NI	Q24 hr	? (P)
					<10	No recommended dosage regimen.		
					<b>Influenza Prophylaxis</b>			
					10–30	NI	Q48 hr	
					<10	No recommended dosage regimen.		
Oxacillin	Renal (hepatic)	23–45 min	Q4–12 hr	D	<10	Use lower range of usual dose.	NI	N (He) N (P)
Penicillin G— and aqueous K <sup>+</sup> Na <sup>+</sup> (IV)	Renal (hepatic)	20–50 min	Q4–6 hr	D	10–50	25% ↓	NI	Y (He)
					<10	50%–80% ↓	NI	? (P)
Penicillin V K <sup>+</sup> (PO)	Renal (hepatic)	30–40 min	Q6–8 hr	I	<10	NI	Q8 hr	Y (He) ? (P)
Pentamidine	Renal	6.4–9	Q24 hr	I	10–30	NI	Q36 hr	N (He)
					<10	NI	Q48 hr	N (P)

Continued

TABLE 31-1

## ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE (Continued)

Drug	Route of Excretion*	Pharmacokinetics		Adjustments in Renal Failure				
		Normal $t_{1/2}$ (hr)	Normal Dose Interval	Method	CrCl (mL/min)	Dose	Interval	Supplemental Dose for Dialysis
Piperacillin	Renal (hepatic)	0.5–1.5	Q4–6 hr	I	20–40	NI	Q8 hr	Y (He)
					<20	NI	Q12 hr	? (P)
Piperacillin/tazobactam	Renal	Piperacillin: 0.5–1.5	Q6–8 hr	D, I	20–40	30% ↓	Q6 hr	? (He)
		Tazobactam: 0.7–1.6			<20	30% ↓	Q8 hr	? (P)
Rifabutin†	Renal (hepatic)	36–45	Q12–24 hr	D	<30	50% ↓	NI	? (He) ? (P)
Rifampin	Hepatic (renal)	1.5–5	Q12–24 hr	D	10–50	50% ↓	NI	N (He)
					<10	50% ↓	NI	Y (P)
Streptomycin sulfate	Renal	2.5	Q24 hr	D, I	50–80	50% ↓	Q24 hr	? (He)
					10–50	50% ↓	Q24–72 hr	? (P)
					<10	50% ↓	Q72–96 hr	
Sulfamethoxazole/trimethoprim	Sulfamethoxazole: hepatic (renal)	Sulfamethoxazole: 9–12	Q12 hr	D	15–30	50% ↓	NI	Y (He)
	Trimethoprim: renal (hepatic)	Trimethoprim: 6–11			<15	Not recommended		? (P)
Sulfisoxazole	Renal	4–8	Q6–12 hr	I	10–50	NI	Q8–12 hr	Y (He)
					<10	NI	Q12–24 hr	Y (P)

TABLE 31-1

## ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE (Continued)

Drug	Pharmacokinetics			Adjustments in Renal Failure				
	Route of Excretion*	Normal $t_{1/2}$ (hr)	Normal Dose Interval	Method	CrCl (mL/min)	Dose	Interval	Supplemental Dose for Dialysis
Tetracycline	Renal (hepatic)	8–10	Q6 hr	I	50–80	NI	Q8–12 hr	N (He)
					10–50	NI	Q12–24 hr	N (P)
					<10	NI	Q24 hr	
Ticarcillin <sup>††</sup>	Renal	0.9–1.3	Q4–6 hr IV	I	10–30	NI	Q8 hr	Y (He)
			Q6–8 hr IM		<10	NI	Q12 hr	? (P)
Ticarcillin/ clavulanate <sup>††</sup>	Renal	Ticarcillin: 0.9–1.3 Clavulanate: 1–1.5	Q4–6 hr	I	10–30	NI	Q8 hr	Y (He)
					<10	NI	Q12 hr	? (P)
					<10 AND hepatic impairment	NI	Q24 hr	
Tobramycin <sup>  </sup>	Renal	1.5–3	Q8–12 hr	I	Any degree of renal insufficiency.	Give usual initial dose and then monitor levels.		Y (He) Y (P) <sup>¶</sup>
Valacyclovir <sup>†</sup>	88% as acyclovir in urine	Valacyclovir: ≈ 30 min Acyclovir: 2–3	Q12–24 hr	D, I	<b>Herpes Zoster (Adults)</b>			Y (He) ? (P)
					30–49	NI	Q12 hr	
					10–29	NI	Q24 hr	
					<10	50% ↓	Q24 hr	
					<b>Genital Herpes (Adol/Adults): Initial Episode</b>			
					10–29	NI	Q24 hr	
					<10	50% ↓	Q24 hr	

Continued

TABLE 31-1

## ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE (Continued)

Drug	Pharmacokinetics			Adjustments in Renal Failure			
	Route of Excretion*	Normal $t_{1/2}$ (hr)	Normal Dose Interval	Method	CrCl (mL/min)	Dose	Interval Supplemental Dose for Dialysis
Valganciclovir (see ganciclovir)					<b>Genital Herpes (Adol/Adults): Recurrent Episode</b>		
					<30	NI	Q24 hr
					<b>Genital Herpes (Adol/Adults): Suppressive</b>		
					<10	500 mg	Q24 hr (for usual dose of 1 g Q24 hr)
						<i>OR</i>	
						500 mg	Q48 hr (for usual dose of 500 mg Q24 hr)
					<b>Herpes Labialis (Adol/Adults)</b>		
					30–49	1 g	Q12 hr × 2 doses
					10–29	500 mg	Q12 hr × 2 doses
					<10	500 mg	Single dose

Valganciclovir  
(see ganciclovir)

TABLE 31-1

## ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE (Continued)

Drug	Route of Excretion*	Pharmacokinetics		Adjustments in Renal Failure				
		Normal $t_{1/2}$ (hr)	Normal Dose Interval	Method	CrCl (mL/min)	Dose	Interval	Supplemental Dose for Dialysis
Vancomycin <sup>  </sup> <b>Note:</b> Alternative would be to give single dose and then check a trough level.	Renal	2.2–8	Q6–12 hr	I	>90	NI	Q6 hr	N (He) <sup>††</sup>
					70–89	NI	Q8 hr	N (P)
					46–69	NI	Q12 hr	
					30–45	NI	Q18 hr	
					15–29	NI	Q24 hr	
					<15	10–20 mg/kg	Subsequent doses best determined by levels.	

\*Route in parentheses indicates secondary route of excretion.

<sup>†</sup>In adults; guidelines not established in children.

<sup>‡</sup>On day 1, normal dose should be given, then decreased for subsequent doses based on renal insufficiency.

<sup>§</sup>After initial loading dose is administered, decrease dose based on renal insufficiency.

<sup>||</sup>Patients on hemodialysis should have a dose of 300 mg or 7 mg/kg/dose at conclusion of each hemodialysis session, with subsequent doses Q48 hr.

<sup>¶¶</sup>With hemodialysis, administer 9 mg/kg (max dose 400 mg) after hemodialysis.

<sup>\*\*\*</sup>For patients on hemodialysis, administer 250 mg after each dialysis session.

<sup>§§§</sup>For patients on hemodialysis, administer 125 mg after each dialysis session.

<sup>§§§§</sup>For patients on hemodialysis: administer 100% of recommended dose after each dialysis session.

<sup>†</sup>Should not use 875-mg tablet or extended-release tablets in patients with CrCl <30 mL/min.

<sup>§</sup>For patients on hemodialysis, administer 3 times a week.

<sup>||</sup>Subsequent doses best determined by measurement of serum levels and assessment of renal insufficiency.

<sup>¶</sup>May add to peritoneal dialysate to obtain adequate serum levels.

<sup>\*\*</sup>GFR ≥ 5 mL/min, give full dose as first dose; GFR < 5 mL/min, give 33% of full dose as first dose.

<sup>††</sup>May inactivate aminoglycosides in patients with renal impairment.

<sup>¶</sup>Rate of acetylation of isoniazid.

Adol, Adolescents; CrCl, creatinine clearance; D, dose reduction; GFR, glomerular filtration rate; He, hemodialysis; I, interval extension; IM, intramuscular; Induct, induction; IV, intravenous; K<sup>+</sup>, potassium; Maint, maintenance; Na<sup>+</sup>, sodium; NI, normal; P, peritoneal dialysis; PO, oral;  $t_{1/2}$ , half-life with normal renal function.



TABLE 31-2

NON-ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE<sup>1-4</sup>

Drug	Route of Excretion*	Pharmacokinetics		Adjustments in Renal Failure				
		Normal $t_{1/2}$ (hr)	Normal Dose Interval	Method	CrCl (mL/min)	Dose	Interval	Supplemental Dose for Dialysis
Acetaminophen	Hepatic	2–4	Q4–6 hr	I	10–50	NI	Q6 hr	N (He)
					<10	NI	Q8 hr	N (P)
Acetazolamide	Renal	2.4–5.8	Q6–24 hr	I	10–50	NI	Q12 hr	Y (He)
					<10	Avoid use		? (P)
Allopurinol	Renal	1–3	Q6–12 hr	D	10–50	50% ↓	NI	? (He)
					<10	70% ↓	NI	? (P)
Aminocaproic Acid	Renal	1–2	Q4–6 hr	D	Oliguria/ESRD	75% ↓	NI	? (He)
								? (P)
Aspirin†	Hepatic (renal)	3–10	Q4 hr	I	10–50	NI	Q4–6 hr	Y (He)
					<10	Avoid use		N (P)
Atenolol	Renal (GI)	3.5–7	Q24 hr	D, I	15–35	1 mg/kg <i>OR</i> 50 mg	Q24 hr	Y (He)
					<15	1 mg/kg <i>OR</i> 50 mg	Q48 hr	N (P)
Azathioprine‡	Hepatic (renal)	0.7–3	Q24 hr	D	10–50	25% ↓	NI	Y (He)
					<10	50% ↓	NI	? (P)
Bismuth subsalicylate	Hepatic (renal)	Salicylate: 2–5 Bismuth: 21–72 days	Q3–4 hr	D	Avoid use in patients with renal failure.			NA
Calcium supplements	GI	Variable	Variable		<25	May require dosage adjustment depending on calcium level.		
Captopril	Renal (hepatic)	1–12.5	Q6–24 hr	D	10–50	25% ↓	NI	Y (He)
					<10	50% ↓	NI	N (P)

TABLE 31-2

## NON-ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE (Continued)

Drug	Route of Excretion*	Pharmacokinetics		Adjustments in Renal Failure				
		Normal $t_{1/2}$ (hr)	Normal Dose Interval	Method	CrCl (mL/min)	Dose	Interval	Supplemental Dose for Dialysis
Carbamazepine	Hepatic (renal)	Initial: 25–65 Subsequent: 8–17	Q6–24 hr	D	<10	25% ↓ (monitor serum levels)	NI	? (He) ? (P)
Cetirizine	Renal (hepatic)	6.2–9	Q12–24 hr	D	<b>&lt;6 yr with Renal Impairment</b> Use not recommended. <b>6–11 yr</b> Any degree of insufficiency. <b>≥12 yr</b> 11–30 <11	   2.5 mg  15 mg Use not recommended.	   Q24 hr  Q24 hr	? (He) ? (P)
Chloral hydrate	Renal	8–11	Q6–8 hr	NA	<50	Avoid use.		NA
Chloroquine	Renal (hepatic)	3–5 days	Q6 hr–7 days	D	<10	50% ↓	NI	N (He) N (P)
Chlorothiazide	Renal	0.75–2	Q12–24 hr	NA	<30	May be ineffective. Use not recommended.		NA
Cimetidine	Renal (hepatic)	1.4–2	Q6–12 hr	D, I	>40 20–40  <20	NI NI OR 25% ↓ NI OR 50% ↓	Q6 hr Q8 hr NI Q12 hr NI	Y (He) ? (P)

Continued

TABLE 31-2

## NON-ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE (Continued)

Drug	Route of Excretion*	Pharmacokinetics		Adjustments in Renal Failure				
		Normal $t_{1/2}$ (hr)	Normal Dose Interval	Method	CrCl (mL/min)	Dose	Interval	Supplemental Dose for Dialysis
Clobazam	Renal (GI)	Children: 16 Adults: 36–42	Q12–24 hr	D	<30	Use with caution; has not been studied.	NI	? (He, P)
Desloratadine	Renal (GI)	27	Q24 hr	I	Any degree of renal impairment	NI	Q48 hr	? (He) ? (P)
Digoxin <sup>§</sup>	Renal	18–48	Q12–24 hr	D, I	<b>Digitalizing Dose</b>			N (He)
					ESRD	50% ↓	NA	N (P)
					<b>Maintenance Dose</b>			
					10–50	25%–75% ↓ OR NI	NI Q36 hr	
Diphenhydramine	Hepatic	2–8	Q4–8 hr	I	<10	75%–90% ↓ OR NI	NI Q48 hr	
					10–50	NI	Q6–8 hr	? (He)
Disopyramide <sup>  </sup>	Renal (GI)	3.15–10	Q6 hr	I	30–40	NI	Q6–12 hr	? (P)
					15–30	NI	Q8 hr	? (He)
					<15	NI	Q12 hr Q24 hr	? (P)
EDTA calcium chloride <sup>  </sup>	Renal	1.5 (IM) 0.3 (IV)	Q4 hr IM Q12 hr IV	D, I	<b>Serum Creatinine: IV Dose</b>			? (He)
					≤2 mg/dL	1 g/m <sup>2</sup>	Q24 hr × 5 days	? (P)
					2–3 mg/dL	500 mg/m <sup>2</sup>	Q24 hr × 5 days	
					3–4 mg/dL	500 mg/m <sup>2</sup>	Q48 hr × 3 doses	
					>4 mg/dL	500 mg/m <sup>2</sup>	Once weekly	

TABLE 31-2

## NON-ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE (Continued)

Drug	Route of Excretion*	Pharmacokinetics		Adjustments in Renal Failure				Supplemental Dose for Dialysis
		Normal $t_{1/2}$ (hr)	Normal Dose Interval	Method	CrCl (mL/min)	Dose	Interval	
Enalapril (IV: enalaprilat)	Renal (hepatic)	1.3–6.3 (PO)	Q6–24 hr	D	10–50	0%–25% ↓	NI	? (He)
		5.1–38 (IV)			<10	50% ↓	NI	N (P)
					Use not recommended in infants and children ≤16 yr with GFR. <30 mL/min/1.73 m <sup>2</sup> .			
Enoxaparin II,†	Renal	4.5–7	Q12 hr	I	<30	NI	Q24 hr	? (He) ? (P)
Famotidine	Renal	0.8–5	Q8–12 hr	D, I	10–50	50% ↓	NI	? (He)
						OR NI	Q24 hr	? (P)
					<10	NI	Q36–48 hr	
Felbamate II	Renal	20–30	Q6–8 hr	D	Any degree of renal impairment.	50% ↓	NI	? (He) ? (P)
Fentanyl	Renal (hepatic)	2–4	Q30 min–1 hr	D	10–50	25% ↓	NI	? (He)
					<10	50% ↓	NI	? (P)
Fexofenadine	GI (renal)	14–18	Q12 hr	I	Any degree of renal impairment.	NI	Q24 hr	? (He) ? (P)
Flecainide	Renal/hepatic	8–27	Q8–12 hr	D	<20	25%–50% ↓	NI	N (He) N (P)
Furosemide	Renal (hepatic)	0.5	Q6–24 hr PO Q6–12 hr IV		Avoid use in oliguric states.			N (He) N (P)

Continued

TABLE 31-2

## NON-ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE (Continued)

Drug	Route of Excretion*	Pharmacokinetics		Adjustments in Renal Failure				Supplemental Dose for Dialysis
		Normal t <sub>1/2</sub> (hr)	Normal Dose Interval	Method	CrCl (mL/min)	Dose	Interval	
Gabapentin <b>  </b>	Renal (hepatic)	4.7–9	Q8 hr	D, I	30–59	200–700 mg	Q12 hr	Y (He)
					15–29	200–700 mg	Q24 hr	N (P)
					<15	100–300 mg	Q24 hr	
Hydralazine <sup>#</sup>	Hepatic (renal)	2–8	Q4–6 hr (IV) Q6–12 hr (PO)	I	10–50	NI	Q8 hr (fast acetylator)	? (He)
					<10	NI	Q8–16 hr Q12–24 hr (slow acetylator)	? (P)
Insulin (regular)**	Hepatic (renal)	1.5	Variable	D	10–50	25% ↓	NI	N (He)
					<10	50%–75% ↓	NI	N (P)
Lacosamide	Renal (GI)	13	Q12 hr	D	<30	Maximum dose 300 mg/24-hr period	NI	Y (He); give 50% dose supplementation after 4-hr He session.
Levetiracetam <b>  </b>	Renal	5–8	Q12 hr	D	Children			Y (He)
					<50	50% ↓	NI	N (P)
					Adults			
					50–80	500–1000 mg	NI	
					30–50	250–750 mg	NI	
					<30	250–500 mg	NI	
	ESRD on dialysis	500–1000 mg	Q24 hr					

TABLE 31-2

## NON-ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE (Continued)

Drug	Route of Excretion*	Pharmacokinetics		Adjustments in Renal Failure				Supplemental Dose for Dialysis
		Normal $t_{1/2}$ (hr)	Normal Dose Interval	Method	CrCl (mL/min)	Dose	Interval	
Lisinopril	Renal	11–13	Q24 hr	D	10–30 <10 Use not recommended for children with CrCl <30 mL/min/1.73 m <sup>2</sup> .	50% ↓ 75% ↓	NI NI	Y (He) N (P)
Lithium	Renal	18–24	Q6–8 hr	D	10–50 <10	25%–50% ↓ 50%–75% ↓	NI NI	Y (He) N (P)
Loratadine	Renal/hepatic	Loratadine: 8.4 Metabolite: 28	Q24 hr	I	<30	NI	Q48 hr	? (He) ? (P)
Meperidine	Renal (hepatic) (normeperidine, renal)	2.3–4	Q3–4 hr	D	10–50 <10	25% ↓ 50% ↓	NI NI	? (He) ? (P)
Methadone	Hepatic (renal)	4–87	Q3–12 hr	D	<10	25%–50% ↓	NI	N (He) N (P)
Methyldopa	Hepatic (renal)	1–3	Q6–12 hr PO Q6–8 hr IV	I	>50 10–50 <10	NI NI NI	Q8 hr Q8–12 hr Q12–24 hr	Y (He) ? (P)
Metoclopramide	Renal	2.5–6	Q6 hr PO Q6–8 hr IV	D	40–50 10–40 <10	25% ↓ 50% ↓ 50%–75% ↓	NI NI NI	? (He) ? (P)
Midazolam	Hepatic (renal)	2.2–6.8	Variable	D	10–29 <10	25% ↓ 50% ↓	NI NI	NA

Continued

TABLE 31-2

## NON-ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE (Continued)

Drug	Route of Excretion*	Pharmacokinetics		Adjustments in Renal Failure				
		Normal t <sub>1/2</sub> (hr)	Normal Dose Interval	Method	CrCl (mL/min)	Dose	Interval	Supplemental Dose for Dialysis
Milrinone	Renal	1.5–3.8	Continuous infusion	D	50 mL/min/1.73 m <sup>2</sup>  40 mL/min/1.73 m <sup>2</sup> 30 mL/min/1.73 m <sup>2</sup> 20 mL/min/1.73 m <sup>2</sup> 10 mL/min/1.73 m <sup>2</sup> 5 mL/min/1.73 m <sup>2</sup>		0.43 mcg/kg/min  0.38 mcg/kg/min 0.33 mcg/kg/min 0.28 mcg/kg/min 0.23 mcg/kg/min 0.2 mcg/kg/min	NA
Morphine	Hepatic (renal)	1–67.8	Variable	D	10–50 <10	25% ↓ 50% ↓	NI NI	? (He) ? (P)
Neostigmine	Hepatic (renal)	0.5–2.1	Variable	D	10–50 <10	50% ↓ 75% ↓	NI NI	? (He) ? (P)
Oxcarbazepine	Renal	Oxcarbazepine: 2 MHD: 9	Q12 hr	D	<30	50% ↓ in initial dose and slower titration	NI	? (He) ? (P)
Pancuronium bromide	Renal (hepatic)	1.8	Q30–60 min OR continuous infusion	D	10–50 <10	50% ↓ Avoid use.	NI	? (He) ? (P)
Phenazopyridine	Renal (hepatic)	?	Q8 hr for 2 days	I	50–80 <50	NI Avoid use.	Q8–16 hr	NA
Phenobarbital	Hepatic (renal, 30%)	37–140	Q8–12 hr	I	<10	NI	Q24 hr	Y (He) Y (P)

TABLE 31-2

## NON-ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE (Continued)

Drug	Route of Excretion*	Pharmacokinetics		Adjustments in Renal Failure				
		Normal $t_{1/2}$ (hr)	Normal Dose Interval	Method	CrCl (mL/min)	Dose	Interval	Supplemental Dose for Dialysis
Primidone	Hepatic (renal, 20%)	Primidone: 10–12 Metabolite: 16	Q6–12 hr	I	>50 10–50 <10	NI NI NI	Q12 hr Q12–24 hr Q24 hr	Y (He) ? (P)
Procainamide	Hepatic (renal)	Procainamide: 1.7–4.7	Q4–6 hr	D	<b>IV (Adult) Maintenance</b> 10–50 <10 <b>IV (Adult) Loading Dose</b> <10	 33% ↓ 67% ↓ 12 mg/kg	 NI NI NA	Y (He) N (P)
Quinidine	Renal	2.5–8	Q4–12 hr	D	<10	25% ↓	NI	Y (He) N (P)
Ranitidine	Renal (hepatic)	1.8–2.5	Q12 hr PO Q6–8 hr IV/IM	D	10–50 <10	50% ↓ 75% ↓	NI NI	N (He) <sup>††</sup> ? (P)
Spironolactone	Renal (hepatic)	Spironolactone: 1.3–1.4	Q6–24 hr	I	10–50 <10	NI Avoid use	Q12–24 hr	NA

Continued



TABLE 31-2

## NON-ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE (Continued)

Drug	Route of Excretion*	Pharmacokinetics		Adjustments in Renal Failure				
		Normal $t_{1/2}$ (hr)	Normal Dose Interval	Method	CrCl (mL/min)	Dose	Interval	Supplemental Dose for Dialysis
Terbutaline	Renal (hepatic)	2.9–14	Variable	D	<50 <10 use not recommended	50% ↓	NI	? (He) ? (P)
Thiopental	Hepatic (renal)	3–11.5	One-time dose	D	<10	25% ↓	NI	NA
Triamterene	Hepatic (renal)	1.6–2.5	Q12–24 hr	I	>50 <50	NI Avoid use	Q12 hr	NA
Verapamil	Renal (hepatic)	2–8	Variable	D	<10 Use caution and closely monitor ECG for PR prolongation, BP, and other signs of overdose.	NI	NI	N (He) N (P)
Vigabatrin (Sabril)	Renal	5–8	Q12 hr	D	50–80	25% ↓	NI	? (He)
					30–50	50% ↓	NI	? (P)
					10–30	75% ↓	NI	

\*Route in parentheses indicates secondary route of excretion.

†With large doses,  $t_{1/2}$  is prolonged up to 30 hours.

‡Azathioprine rapidly converted to mercaptopurine ( $t_{1/2}$  = 0.5–4 hours).

§Decrease loading dose by 50% in end-stage renal disease because of decreased volume of distribution.

||Guidelines for adults; guidelines not established for children.

\*Closely monitor antifactor Xa.

#Dose interval varies for rapid and slow acetylators with normal and impaired renal function.

\*\*Renal failure may cause hyposensitivity or hypersensitivity to insulin; adjust to clinical response and blood glucose.

††Adjust dose schedule to administer dose at end of dialysis.

BP, Blood pressure; CrCl, creatinine clearance; D, dose reduction; EDTA, ethylenediaminetetraacetic acid; ECG, electrocardiogram; ESRD, end-stage renal disease; GFR, glomerular filtration rate; GI, gastrointestinal; He, hemodialysis; I, interval extension; IM, intramuscular; IV, intravenous; MHD, 10-monohydroxy metabolite; NA, not applicable; NI, normal; P, peritoneal dialysis; PO, oral;  $t_{1/2}$ , half life.

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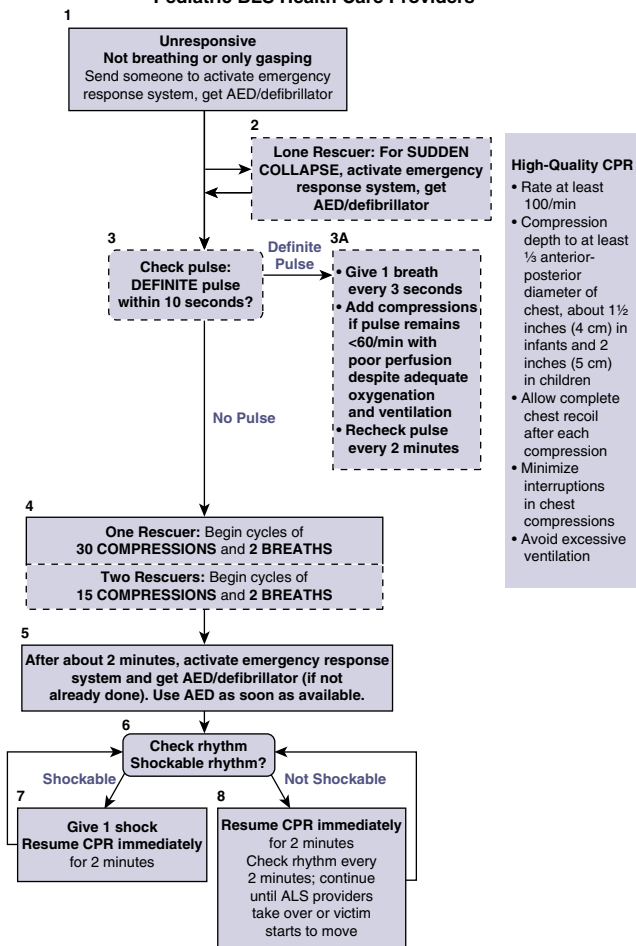
Zyrtec. *See* Cetirizine

Zyrtec-D 12 Hour. *See* Cetirizine and pseudoephedrine

Zyvox. *See* Linezolid

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## Pediatric BLS Health Care Providers

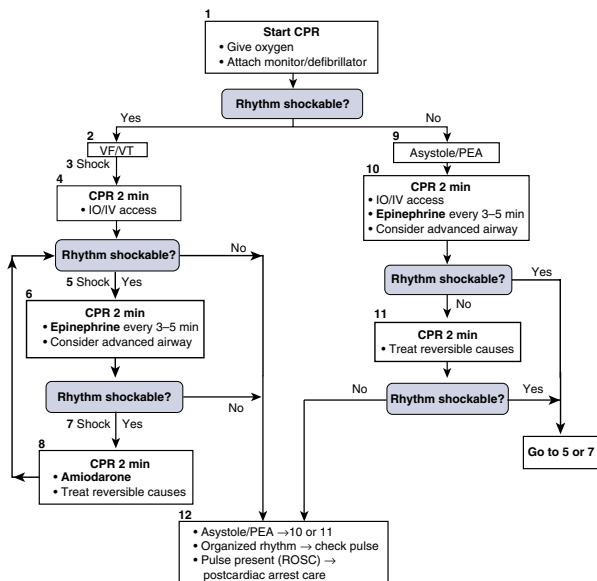


*Note:* The boxes bordered with dashed lines are performed by health care providers and not by lay rescuers

Pediatric BLS health care providers algorithm. Reprinted with permission. 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Part 13. Circulation. 2010;122:S862-S875. © 2010 American Heart Association, Inc.

## Pediatric Cardiac Arrest

### Shout for Help/Activate Emergency Response



### Doses/Details

#### CPR Quality

- Push hard ( $\geq \frac{1}{2}$  of anterior-posterior diameter of chest) and fast (at least 100/min) and allow complete chest recoil
- Minimize interruptions in compressions
- Avoid excessive ventilation
- Rotate compressor every 2 minutes
- If no advanced airway, 15:2 compression-ventilation ratio. If advanced airway, 8–10 breaths per minute with continuous chest compressions

#### Shock Energy for Defibrillation

First shock 2 J/kg, second shock 4 J/kg, subsequent shocks  $\geq 4$  J/kg, maximum 10 J/kg or adult dose.

#### Drug Therapy

- **Epinephrine IO/IV Dose:** 0.01 mg/kg (0.1 mL/kg of 1:10 000 concentration). Repeat every 3–5 minutes. If no IO/IV access, may give endotracheal dose: 0.1 mg/kg (0.1 mL/kg of 1:1000 concentration).
- **Amiodarone IO/IV Dose:** 5 mg/kg bolus during cardiac arrest. May repeat up to 2 times for refractory VF/pulseless VT.

#### Advanced Airway

- Endotracheal intubation or supraglottic advanced airway
- Waveform capnography or capnometry to confirm and monitor endotracheal tube placement
- Once advanced airway in place give 1 breath every 6–8 seconds (8–10 breaths per minute)

#### Return of Spontaneous Circulation (ROSC)

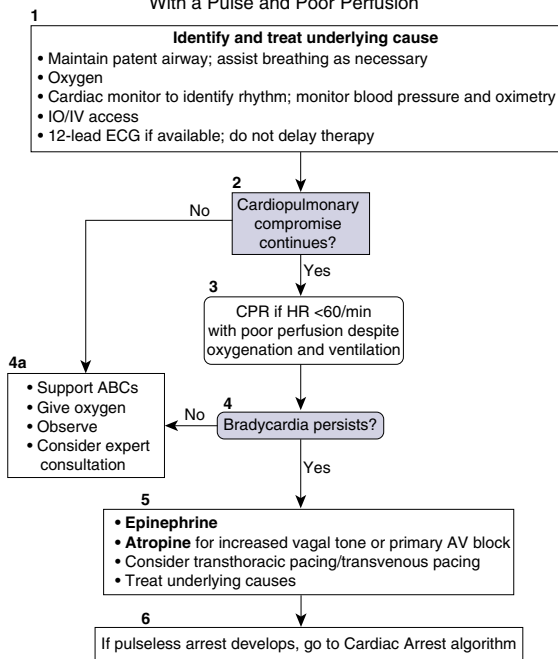
- Pulse and blood pressure
- Spontaneous arterial pressure waves with intra-arterial monitoring

#### Reversible Causes

- |                            |                         |
|----------------------------|-------------------------|
| – Hypovolemia              | – Tension pneumothorax  |
| – Hypoxia                  | – Tamponade, cardiac    |
| – Hydrogen ion (acidosis)  | – Toxins                |
| – Hypoglycemia             | – Thrombosis, pulmonary |
| – Hypokalemia/hyperkalemia | – Thrombosis, coronary  |
| – Hypothermia              |                         |



## Pediatric Bradycardia With a Pulse and Poor Perfusion



### Cardiopulmonary Compromise

- Hypotension
- Acutely altered mental status
- Signs of shock

#### Doses/Details

**Epinephrine IO/IV Dose:** 0.01 mg/kg (0.1 mL/kg of 1:10,000 concentration). Repeat every 3–5 minutes. If IO/IV access not available but endotracheal (ET) tube in place, may give ET dose: 0.1 mg/kg (0.1 mL/kg of 1:1000).

**Atropine IO/IV Dose:** 0.02 mg/kg. May repeat once. Minimum dose 0.1 mg and maximum single dose 0.5 mg.

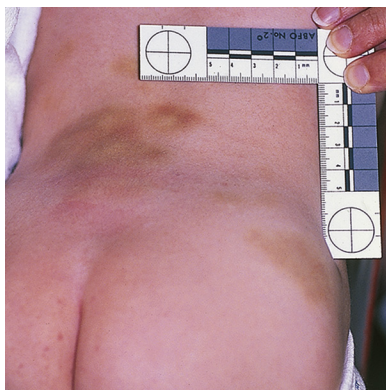
Pediatric bradycardia algorithm. Reprinted with permission. 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Part 14: Pediatric advanced life support. Circulation. 2010;122:S887. © 2010 American Heart Association, Inc.

**FIGURE 4-5**

Infant whose lower extremities and buttocks have been burned when immersed in hot water. (From Zitelli B, Davis H. Atlas of Pediatric Physical Diagnosis. 5th ed. St Louis: Mosby, 2008.)

**FIGURE 4-6**

Child who has been beaten with a looped cord. (From Zitelli B, Davis H. Atlas of Pediatric Physical Diagnosis. 5th ed. St Louis: Mosby, 2008.)

**FIGURE 4-7**

Child with suspicious bruising on lower back. (From Zitelli B, Davis H. Atlas of Pediatric Physical Diagnosis. 5th ed. St Louis: Mosby, 2008.)

**FIGURE 4-8**

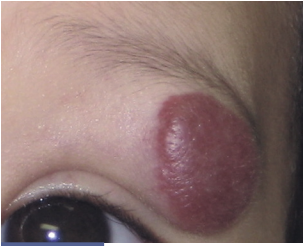
Toddler slapped in the face, with linear hand marks visible. (From Zitelli B, Davis H. *Atlas of Pediatric Physical Diagnosis*. 5th ed. St Louis: Mosby; 2008.)

**FIGURE 4-9**

Skin burned with hot cigarette lighter. (From Zitelli B, Davis H. *Atlas of Pediatric Physical Diagnosis*. 5th ed. St Louis: Mosby; 2008.)

**FIGURE 4-10**

Child beaten with a switch. (From Zitelli B, Davis H. *Atlas of Pediatric Physical Diagnosis*. 5th ed. St Louis: Mosby; 2008.)

**FIGURE 8-2**

Infantile hemangioma.

**FIGURE 8-3**

Molluscum contagiosum. (From Cohen BA. *Pediatric Dermatology*. 3rd ed. St Louis: Mosby, 2005:126.)

**FIGURE 8-4**

Pyogenic granuloma. (From Cohen BA. *Dermatology Image Atlas*. Available at <http://www.dermatlas.org/>, 2001.)

**FIGURE 8-5**

Scabies.

**FIGURE 8-7**

Herpetic gingivostomatitis. (From Cohen BA. *Pediatric Dermatology*. 3rd ed. St Louis: Mosby, 2005: 103.)



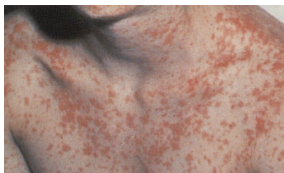
**FIGURE 8-8**

Herpes zoster. (From Cohen BA. *Pediatric Dermatology*. 3rd ed. St Louis: Mosby, 2005:106.)



**FIGURE 8-9**

Varicella. (From Cohen BA. *Pediatric Dermatology*. 3rd ed. St Louis: Mosby, 2005:104.)



**FIGURE 8-10**

Measles. (From Cohen BA. *Pediatric Dermatology*. 3rd ed. St Louis: Mosby, 2005:166.)



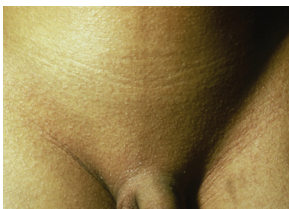
**FIGURE 8-11**

Fifth disease. (From Cohen BA. *Pediatric Dermatology*. 3rd ed. St Louis: Mosby, 2005:167.)



**FIGURE 8-12**

Roseola. (From Cohen BA. *Pediatric Dermatology*. 3rd ed. St Louis: Mosby, 2005: 168.)



**FIGURE 8-13**

Scarlet fever. (From Cohen BA. *Dermatology Image Atlas*. Available at <http://www.dermatlas.org>, 2001.)

**FIGURE 8-15**

Psoriasis. (From Cohen BA. *Pediatric Dermatology*. 3rd ed. St Louis: Mosby, 2005:67.)

**FIGURE 8-16**

Keratosis pilaris. (From Cohen BA. *Pediatric Dermatology*. 3rd ed. St Louis: Mosby, 2005:81.)

**FIGURE 8-17**

Tinea corporis. (From Cohen BA. *Pediatric Dermatology*. 3rd ed. St Louis: Mosby, 2005:94.)

**FIGURE 8-18**

Tinea pedis. (From Cohen BA. *Dermatology Image Atlas*. Available at <http://www.dermatlas.org>, 2001.)

**FIGURE 8-19**

Pityriasis rosea. (From Cohen BA. *Pediatric Dermatology*. 3rd ed. St Louis: Mosby, 2005:87.)





**FIGURE 8-20**

Pityriasis alba. (From Cohen BA. Pediatric Dermatology. 3rd ed. St Louis: Mosby, 2005:82.)



**FIGURE 8-21**

Postinflammatory hyperpigmentation. (From Cohen BA. Atlas of Pediatric Dermatology. St Louis: Mosby, 1993.)



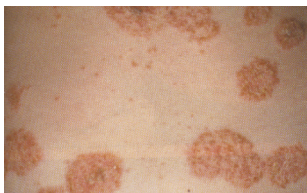
**FIGURE 8-22**

Infantile eczema. (From Cohen BA. Pediatric Dermatology. 3rd ed. St Louis: Mosby, 2005:79.)



**FIGURE 8-23**

Childhood eczema. (From Cohen BA. Dermatology Image Atlas. Available at [www.med.jhu.edu/peds/dermatlas](http://www.med.jhu.edu/peds/dermatlas), 2001.)



**FIGURE 8-24**

Nummular eczema. (From Cohen BA. Pediatric Dermatology. 3rd ed. St Louis: Mosby, 2005:80.)



**FIGURE 8-25**

Follicular eczema. (From Cohen BA. Pediatric Dermatology. 3rd ed. St Louis: Mosby, 2005:80.)

**FIGURE 8-26**

Childhood eczema with lesion in suprapubic area. (From Cohen BA. *Pediatric Dermatology*. 3rd ed. St Louis: Mosby, 2005, Fig. 3.20c.)

**FIGURE 8-27**

Papular urticaria. (From Cohen BA. *Dermatology Image Atlas*. Available at <http://www.dermatlas.org>, 2001.)

**FIGURE 8-28**

Congenital ichthyosis erythroderma. (From Cohen BA. *Pediatric Dermatology*. 3rd ed. St Louis: Mosby, 2005:79.)

**FIGURE 8-29**

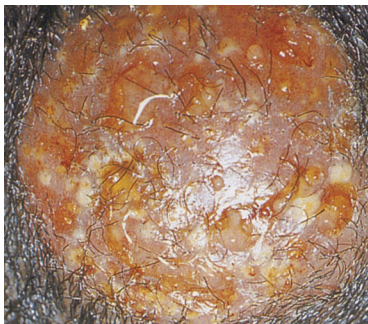
Tinea versicolor. (From Cohen BA. *Atlas of Pediatric Dermatology*. St Louis: Mosby, 1993.)





**FIGURE 8-30**

Tinea capitis. (From Cohen BA. Atlas of Pediatric Dermatology. St Louis: Mosby, 1993.)



**FIGURE 8-31**

Kerion. (From Cohen BA. Pediatric Dermatology. 3rd ed. St Louis: Mosby, 2005:207.)



**FIGURE 8-32**

Alopecia areata. (From Cohen BA. Pediatric Dermatology. 3rd ed. St Louis: Mosby, 2005:208.)



**FIGURE 8-33**

Telogen effluvium. (From Cohen BA. Dermatology Image Atlas. Available at [www.med.jhu.edu/peds/dermatlas](http://www.med.jhu.edu/peds/dermatlas), 2001.)



**FIGURE 8-34**

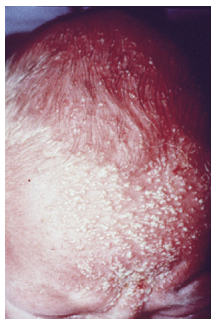
Traction alopecia. (From Cohen BA. Pediatric Dermatology. 3rd ed. St Louis: Mosby, 2005: 209.)

**FIGURE 8-36**

Erythema toxicum neonatorum. (From Cohen BA. *Pediatric Dermatology*. 2nd ed. St Louis: Mosby, 1999:18.)

**FIGURE 8-38**

Hyperpigmentation from resolving transient neonatal pustular melanosis. (From Cohen BA. *Pediatric Dermatology*. 3rd ed. St Louis: Mosby, 2005:20.)

**FIGURE 8-37**

Transient neonatal pustular melanosis. (From Cohen BA. *Pediatric Dermatology*. 3rd ed. St Louis: Mosby, 2005:20.)

**FIGURE 8-39**

Miliaria rubra. (From Cohen BA. *Pediatric Dermatology*. 3rd ed. St Louis: Mosby, 2005:22.)

**FIGURE 8-40**

Milia. (From Cohen BA. *Pediatric Dermatology*. 3rd ed. St Louis: Mosby, 2005:22.)

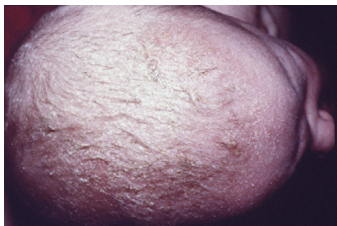
**FIGURE 8-41**

Neonatal acne. (From Cohen BA. *Pediatric Dermatology*. 3rd ed. St Louis: Mosby, 2005:23.)



**FIGURE 8-42**

Seborrheic dermatitis. (From Cohen BA. *Pediatric Dermatology*. 3rd ed. St Louis: Mosby, 2005:33.)



**FIGURE 8-43**

Seborrheic dermatitis. (From Cohen BA. *Pediatric Dermatology*. 3rd ed. St Louis: Mosby, 2005:33.)



**FIGURE 8-44**

Diaper candidiasis. (From Cohen BA. *Pediatric Dermatology*. 3rd ed. St Louis: Mosby, 2005:34.)



**FIGURE 8-45**

Pemphigus vulgaris. (From Cohen BA. *Dermatology Image Atlas*. Available at [www.dermatlas.org](http://www.dermatlas.org), 2001.)



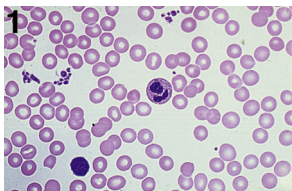
**FIGURE 8-46**

Allergic contact dermatitis. (From Cohen BA. *Pediatric Dermatology*. 3rd ed. St Louis: Mosby, 2005:75.)

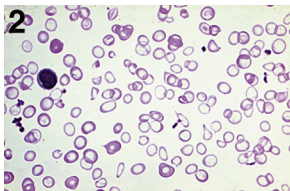


**FIGURE 8-47**

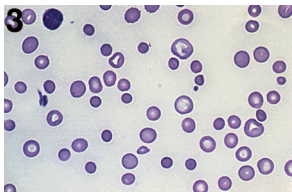
Poison ivy. (From Cohen BA. *Dermatology Image Atlas*. Available at <http://www.med.jhu.edu/peds/dermatlas>, 2001.)

**FIGURE 14-4**

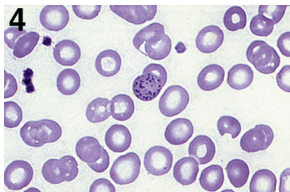
Normal smear. Round RBCs with central pallor about one third of the cell's diameter, scattered platelets, occasional white blood cells.

**FIGURE 14-5**

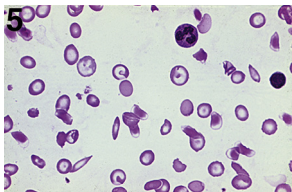
Iron deficiency. Hypochromic/microcytic RBCs, poikilocytosis, plentiful platelets, occasional ovalocytes and target cells.

**FIGURE 14-6**

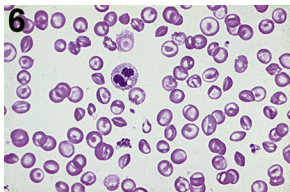
Spherocytosis. Microspherocytes a hallmark (densely stained RBCs with no central pallor).

**FIGURE 14-7**

Basophilic stippling as a result of precipitated RNA throughout the cell; seen with heavy metal intoxication, thalassemia, iron deficiency, and other states of ineffective erythropoiesis.

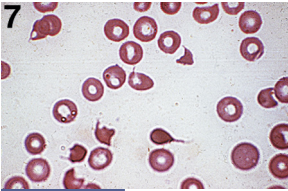
**FIGURE 14-8**

Hemoglobin SS disease. Sickled cells, target cells, hypochromia, poikilocytosis, Howell-Jolly bodies; nucleated RBCs common (not shown).

**FIGURE 14-9**

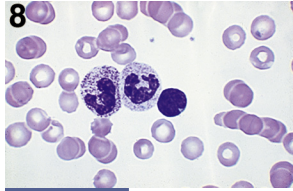
Hemoglobin SC disease. Target cells, oat cells, poikilocytosis; sickle forms rarely seen.





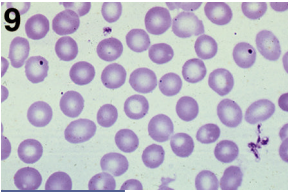
**FIGURE 14-10**

Microangiopathic hemolytic anemia. RBC fragments, anisocytosis, polychromasia, decreased platelets.



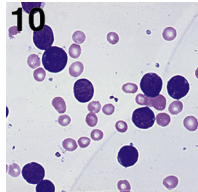
**FIGURE 14-11**

Toxic granulations. Prominent dark blue primary granules; commonly seen with infection and other toxic states (e.g., Kawasaki disease).



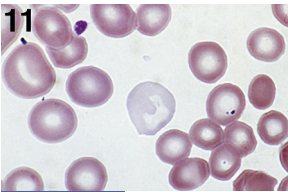
**FIGURE 14-12**

Howell-Jolly body. Small, dense nuclear remnant in an RBC; suggests splenic dysfunction or asplenia.



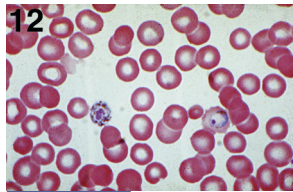
**FIGURE 14-13**

Leukemic blasts showing large nucleus-to-cytoplasm ratio.



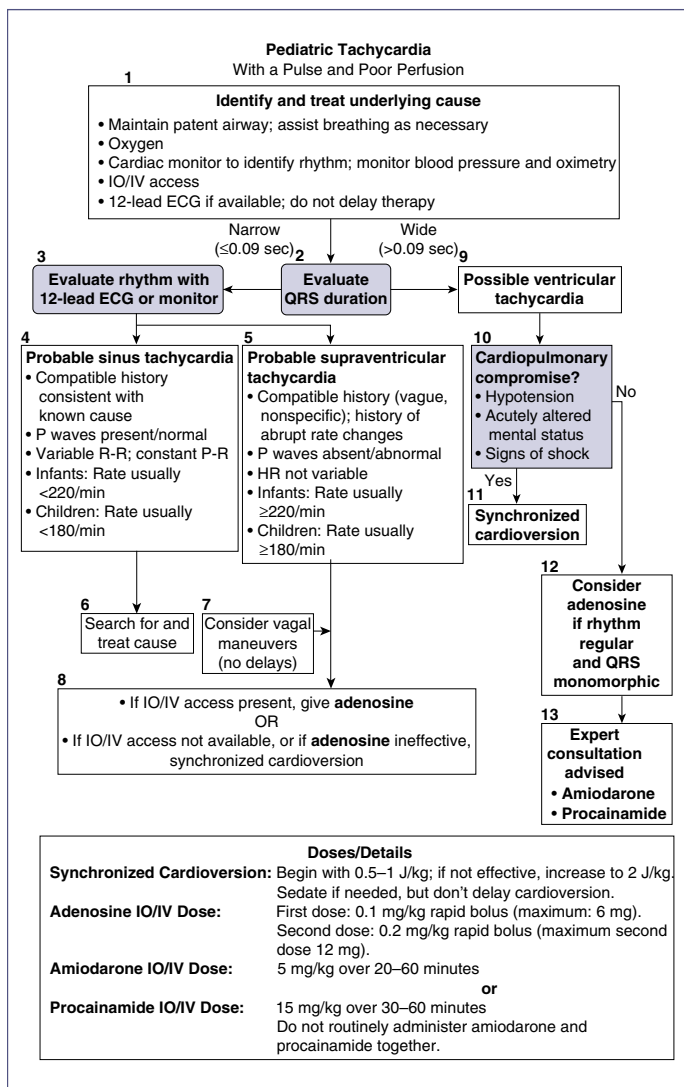
**FIGURE 14-14**

Polychromatophilia. Diffusely basophilic because of RNA staining; seen with early release of reticulocytes from the marrow.



**FIGURE 14-15**

Malaria. Intraerythrocytic parasites.



Pediatric tachycardia algorithm. Reprinted with permission. 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Part 14: Pediatric advanced life support. Circulation. 2010;122:S888. © 2010 American Heart Association, Inc.